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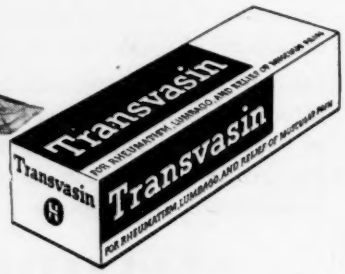

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IDIOPATHIC THROMBOCYTOPENIC PURPURA

A CHALLENGE*

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Werlhof (1735) is said to have been the first to describe what is now called idiopathic thrombocytopenic purpura (I.T.P.). Under the name "Morbus maculosus hæmorrhagicus" he reported in a few lines the case of a girl, previously healthy, who suddenly broke out in a hæmorrhagic rash and had severe mucosal bleeding. The illness receded as quickly as it had come, and within a week little trace of the purpura was evident. Werlhof could offer no clue to the cause of this severe ailment, and even today, some 200 years later, the causes of I.T.P. are by no means clear. This does not mean that progress has not been made; in the past few years several striking developments have taken place that have gone far to revolutionise our concepts of this disease.

Originally our thinking centred on the remarkable effects of splenectomy and on the megakaryocytic changes; thus I.T.P. was conceived of as a form of hypersplenism (Dameshek and Miller 1946). More recently our preoccupation with immunological mechanisms in hæmolytic diseases (Dameshek 1950) has led naturally to a consideration of similar mechanisms in I.T.P. and other diseases. This has come about not only through a consideration of the striking differences between acute and chronic I.T.P. but also through actual determination of an extrinsic, and presumably immunological, mechanism affecting the blood-platelets, similar to the auto-immune mechanisms in acquired hæmolytic anæmia. Despite the increased emphasis on the immunological aspects of I.T.P., the important rôle of the spleen, particularly in the chronic cases, remains a subject for discussion, particularly in view of the striking effects of splenectomy on the production of platelets from their megakaryocytic precursors in the bone-marrow.

Previous Theories

Most of the theories advanced to interpret the pathogenesis of I.T.P. have attempted to explain two characteristic features of the disease: (1) the thrombocytopenia in the peripheral blood in the presence of normal or increased number of megakaryocytes in the bone-marrow; and (2) the often beneficial effect of splenectomy.

Megakaryocytes.—The interpretation of the morphology and the apparent functional activity of the megakaryocytes remains controversial. To some observers (Frank 1915, 1925, Dameshek and Miller 1946) the megakaryocytes not only are increased in number but may be grossly abnormal (lack of granularity of the cytoplasm at the peripheral area; lack of platelet formation; vacuolisation of nucleus and cytoplasm). These changes have been thought to be due to the influence of an abnormal humoral substance emanating from the spleen. The striking changes in the granularity of the megakaryocytes and their greatly accelerated platelet production following successful splenectomy have been offered as evidence to support this view. Other workers (Wiseman et al. 1940) consider that the thrombocytopenia is due to the destruction of platelets in the spleen either by lysis or by "selective sequestration" and phagocytosis (Doan 1949). Another totally different concept is that of Tidy (1926), who suggested that the thrombocytopenia of I.T.P. is due to increased utilisation of platelets at the periphery, presumably to prevent leakage of blood from injured capillaries. Tidy's hypothesis focuses attention on one of the outstanding features of the acute cases of I.T.P., in which capillary injury is probably present simultaneously with the thrombocytopenia.

Spleen.—At least until recent years emphasis has been laid on the central rôle of the spleen in the pathogenesis of I.T.P., whether by inhibiting formation and release of platelets or by the direct (or indirect) destruction of platelets. Certain confirmatory findings point to splenic dysfunction—i.e., the behaviour of extracts from spleen of patients with I.T.P. These extracts have been stated to contain substances depressing the platelet-count in laboratory animals (thrombocytopen: Troland and Lee 1938, Torrioli and Puddu 1938). This work has been further extended in the attempt to show that even the normal spleen contains at least two principles through which the production, delivery, and level of circulating platelets may be regulated (Moolten 1945). These various observations are difficult to confirm, and their exact significance must remain at present sub judice.

I.T.P. not a Single Syndrome

Unfortunately none of the various theories could explain all cases of I.T.P. Not infrequently recovery took place spontaneously without splenectomy, or even some time after an apparently unsuccessful splenectomy. In other cases splenectomy appeared temporarily successful, but thrombocytopenia recurred shortly afterwards. Analysis of the natural history of many cases of I.T.P. showed that they varied greatly in onset, course, and clinical findings. Gradually it became clear that I.T.P. could hardly be viewed as a simple unitary syndrome. Thus, Hirsch and Dameshek (1951) have pointed to the striking differences between acute and chronic cases and to their differing ætiology, prognosis, and therapeutic implications. It is usually possible to distinguish between the "acute" self-limited cases and the "chronic" ones on the basis of onset, clinical picture, duration, outcome, and, very likely, pathogenic mechanism.

Acute I.T.P.—Patients with the "acute" disease, as in Werlhof's famous case, usually present a sudden onset of bleeding into the skin and from mucosæ, without previous history of bleeding. A history of recent infection or of the intake of drugs is often obtained. Possibly the capillary walls, as well as the platelets, are directly involved by the pathogenic agent, as the result of which the bleeding-time becomes greatly prolonged and the capillary fragility increased. The bleeding is severe, but a few days later, as the capillary involvement declines, bleeding becomes greatly reduced, although

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TABLE I—DIFFERENTIATION BETWEEN ACUTE SELF-LIMITED AND CHRONIC I.T.P.

—	Acute I.T.P.	Chronic I.T.P.
Familial history ..	Occasional easy bruising	Occasional thrombocytopenia; more commonly, easy bruising
Past history	None	Easy bruising or other abnormal tendency to bleed present for years
Ætiological factors ..	Infection; drugs (antibiotics, antihistaminics, &c.)	Platelet agglutinins, ? unknown
Physical findings ..	Severe purpura	Less severe purpura; splenomegaly in 20–30% of cases
Blood findings besides thrombocytopenia	Lymphocytosis, especially in children and often eosinophilia; rare platelets, normal morphology	Platelets large, agranular, and bizarre; no other findings of diagnostic significance
Bone-marrow findings	Lymphocytosis and occasional eosinophilia; number of megakaryocytes normal or slightly increased; no evidence of platelet formation and insufficient granularity of cytoplasm of megakaryocytes, which tend to be of primitive type (megakaryoblasts, promegakaryocytes)	Number of megakaryocytes increased, at times greatly; no evidence of platelet formation and granularity at periphery of cell; otherwise normal in perinuclear area; megakaryocytes more mature (intermediate and adult forms)
"Survival time" of injected platelets	1–2 hours	12–36 hr. or, seldom, longer
Electrophoretic pattern (Bernfeld and Stefanini 1951)	Presence of α_2 globulin	No characteristic findings
Thrombocytopenic effect of transfusion of patient's plasma into normal people	None,* in most cases	Variable, but often present (about 60% of cases)
Circulating platelet agglutinins	None (rare exceptions)	In about half the cases
Course	Acute, self-limited; death due to severe uncontrollable bleeding, or spontaneous recovery within 4 mos.	Chronic, with failure of platelet-count to reach completely normal values; frequent exacerbations, especially at menstrual period
Treatment	Supportive: corticotrophin, and platelet transfusions value of splenectomy difficult to assess	Splenectomy successful in $^2/_3$ of cases; corticotrophin and platelet transfusions useful to tide over a crisis, or as preparation for splenectomy

* Not greater than the ordinary thrombocytopenic effect due to normal plasma.

the thrombocytopenia is unmodified. Still later the purpura subsides altogether; shortly afterwards the platelet-count begins to rise; and a permanent remission becomes established. *Although in some cases the process seems to evolve into the chronic disease*, usually the acute disorder has a self-limited course lasting from a few weeks to a few months.

Chronic I.T.P.—In the "chronic" type of I.T.P. the course is prolonged and marked by remissions and relapses. The bleeding, even in the fully active cases, is usually less severe, probably because involvement of capillaries is minimal or absent. Other differential criteria between "acute" and "chronic" I.T.P. are presented in table I. In "chronic" I.T.P. the platelets present evident morphological abnormalities and may be shown to be functionally abnormal. In some of the chronic cases ("thrombocytopathic thrombocytopenic purpura") the platelet-count may be only slightly subnormal, but the platelets are grossly abnormal both in appearance and in function. Finally, there are cases of thrombocytopenic purpura, apparently idiopathic, which reveal at splenectomy a previously unrecognised disease of the spleen: tuberculosis, lupus erythematosus, Gaucher's disease, &c.[1] This "hypersplenic" type of I.T.P. may simulate either the "acute" or the "chronic" type of the disease.

Immunology

In the past few years, as advance has quickly followed advance, our understanding of the pathogenesis of I.T.P. has become almost completely revolutionised, with the result that the explanations based on hypersplenism have shifted to those dealing with immunological or immuno-allergic mechanisms.

The observations of Grandjean (1948) and of Ackroyd (1949a and b) on the mechanism of quinine purpura and 'Sedormid' purpura respectively have contributed greatly towards the clarification of the pathogenesis of this type of acute I.T.P. Ackroyd demonstrated clearly that the sudden and severe thrombocytopenia of sedormid purpura was due to the destruction (lysis) of platelets within the circulation. In-vitro studies indicated that this mechanism required, in addition to platelets, the presence of (1) the offending drug, (2) complement, and (3) a fraction of the patient's plasma. An additional mechanism operating in vivo might be represented by inhibition of platelet release and even platelet formation from the megakaryocytes.

Fisher (1947) and Evans et al. (1951) have emphasised the many similarities and analogies between I.T.P. and acquired hæmolytic anæmia of the auto-immune type in some patients. Evans et al. (1951) have also pointed to the not infrequent presence of both disorders simultaneously, and indicated that positive anti-globulin tests were often present in I.T.P. These observers have also described platelet agglutinins in the serum of patients with I.T.P. and, after some discussion about the technical precautions necessary to prevent non-specific agglutination of platelets by pathological sera (Stefanini and Silverberg 1951), the presence of agglutinins in selected cases has been confirmed by Stefanini et al. (1952a) and Harrington et al. (1952).

One variety of thrombocytopenia of the newborn occurs in children born of mothers suffering from the chronic type of I.T.P. or previously successfully splenectomised. Thrombocytopenia of the newborn remits spontaneously some time after birth. On the basis of this and other findings Epstein et al. (1950) postulated that the thrombocytopenia might be due to the passage of a thrombocytopenia-inducing agent from the maternal to the fœtal circulation. Harrington et al. (1951a and b) showed that the plasma of patients with I.T.P. produced, when injected into normal people, various degrees of thrombocytopenia,[2] lasting from a few hours to several days and occasionally accompanied by clinical purpura. They found that the activity of the plasma was due to a globulin which could even be detected in the plasma of patients successfully splenectomised for I.T.P.

The presence of an extrinsic factor in the blood causing destruction of platelets has been further demonstrated by studies on the rate of disappearance of "survival time" of platelets injected into the circulation of patients

1. As our knowledge extends, the term "idiopathic" will probably be used less and less with reference to thrombocytopenic purpura. An acceptable definition for the disease may then be that of "megakaryocytic thrombocytopenic purpura," compared to "amegakaryocytic (or secondary) thrombocytopenic purpura" (as in leukæmia, aplastic anæmia, &c.), where the bone-marrow shows extreme lack of megakaryocytes.

2. The thrombocytopenia which follows the administration of plasma from patients with I.T.P. should not be confused with the moderate and transitory drop in platelet-count occurring in about 80% of normal people after the administration of normal plasma (Stefanini and Chatterjea 1952).

with various thrombocytopenic states. Platelets injected into patients who have never before had a transfusion [3] and who have "amegakaryocytic" thrombocytopenia (as in aplastic anæmia and in leukæmia), survive from four to six days (Stefanini and Chatterjea 1951, Stefanini et al. 1952c, Hirsch and Gardner 1951, 1952). The survival time of platelets, however, is only a matter of a few hours in acute I.T.P., and $^1/_2$–1 day in chronic I.T.P. This observation represents the only constant finding indicating that an extrinsic platelet destructive mechanism of varying intensity is to be found in all cases of I.T.P.

These studies have shown that it is possible to recognise certain significant differences in mechanism between "acute" and "chronic" types of I.T.P. In addition, it is becoming possible to build up laboratory as well as clinical distinctions between the acute and chronic types (table 1). Thus our studies have indicated that the plasma of patients with "acute I.T.P." does not induce severe thrombocytopenia in normal recipients, and only seldom contains demonstrable platelet agglutinins. Studies at operation have shown that there is no "selective sequestration" of platelets in the spleen (Stefanini et al. 1952b), since platelets are retained by the spleen at no greater rate and in no higher number than they are in other parenchymal organs or in other pathological states, or in normal spleens. Nevertheless, since the onset of thrombocytopenia is extremely sudden and the injected platelets disappear extremely rapidly, the existence of some type of mechanism of destruction of platelets is quite clear. Examination of the megakaryocytes reveals no such great increase in these cells as that noted in chronic I.T.P., but rather striking morphological abnormalities and degenerative changes of the nucleus and cytoplasm are often present. Electrophoretic studies of the serum (Bernfeld and Stefanini 1951) have revealed an abnormal globulin, which we have named alpha-x globulin, and which is also seen, peculiarly enough, in hæmophilia, anaphylactoid purpura, and certain hæmolytic diseases with thrombocytopenia. It is postulated that the acute cases may be due to a different type of immunological mechanism than that in the chronic cases, perhaps a form of allergy, possibly related to the development of hypersensitivity to certain chemicals [4] or to certain bacterial and viral products. Although the nature of the sensitising agent remains unknown, the clinical and laboratory picture of acute I.T.P. is very close to that of thrombocytopenic purpura due to demonstrable drug sensitivity (sedormid, quinidine, &c.). A major difference is, however, that in quinidine purpura and sedormid purpura the course is much more limited. Even the "survival time" of platelets injected into a patient with quinidine thrombocytopenic purpura is found to be normal as soon as the plasma quinidine has fallen to a low level (G. I. Plitman and M. Stefanini, unpublished observations).

Owing to the striking tendency to spontaneous recovery, the assessment of any form of treatment in the "acute" form of I.T.P. is particularly difficult. Splenectomy may fail to affect the course of the disease altogether, or it may be followed by a remission. In the latter case the possibility remains, of course, that the remission might have been spontaneous or accelerated by splenectomy. It is, in fact, conceivable that the presence of the spleen might retard the increase in the platelet-count during spontaneous recovery from acute I.T.P. and, once that organ has been removed there will be a sudden increase in platelets. As emphasised by several workers, corticotrophin and, probably to a lesser extent, cortisone affect favourably the course of the I.T.P. more by reducing or controlling the vascular component of purpura than by influencing the platelet-count. The relationship of "acute" I.T.P. to some cases of acquired hæmolytic anæmia has already been emphasised. Cases of "acute" I.T.P. which do not respond to any form of therapy, including splenectomy, may conceivably be related to the complex hæmolytic-thrombocytopenic-thrombotic disease known as "thrombotic thrombocytopenic purpura." The latter condition may, in turn, be allied to lupus erythematosus and periarteritis nodosa.

An apparently different ætiological problem is met in the "chronic" variety of I.T.P. Platelet agglutinins are found in about half these patients, and in almost every instance the plasma of these patients containing agglutinins induces severe thrombocytopenia when injected into normal recipients. It is, of course, possible that our present techniques fail to reveal the presence of platelet agglutinins in cases where they are present in minimal concentration; this may also explain the lack of thrombocytopenic activity in vivo of plasma not showing agglutinating activity in vitro. When present, the platelet agglutinin may explain most, if not all, of the features of chronic I.T.P. Our studies (Stefanini et al. 1953) have indicated that a platelet agglutinin, if present in sufficiently high titre, can (1) lead to the destruction of circulating platelets; (2) free the surface of the megakaryocyte of the platelets and inhibit their release from the parent cell; and (3) produce degenerative changes of the megakaryocyte itself, which would ultimately lead to cessation of platelet production (Pisciotta et al. 1953).

The rôle of the spleen in the cases of chronic I.T.P. with circulating platelet agglutinins is still a moot question. In one case, with an extremely high titre of platelet agglutinin, splenectomy, although producing an improvement of the bleeding, failed to reduce both the agglutinin titre and the thrombocytopenic effect of the patient's plasma injected into normal people. The platelet-count was, however, increased temporarily after the operation. From these results it seems that the spleen has at most a minor rôle in the elaboration of the platelet agglutinin, but that it may coöperate in the destruction or disposal of platelets sensitised or injured by the platelet agglutinin. Removal of the spleen may thus be followed by a temporary rise in the platelet-count until, at a later date, the functions of the spleen are taken over by other sections of the reticulo-endothelial system. This interpretation is perhaps supported by the experimental findings of Elliott and Whipple (1940), who found that the injection of heterologous anti-platelet serum in relatively small amount would not induce thrombocytopenia in a recently splenectomised animal, but that with a large amount of serum there was no effect from splenectomy. The striking and often permanent effects of splenectomy in most cases of chronic I.T.P. cannot, in fact, be explained on the basis of the removal of an abnormal immunological mechanism, but seem to indicate the presence of a substance within the spleen having a distant suppressive effect, via the blood-stream, on the production and delivery of the platelets by the megakaryocytes. In this rôle the place of the spleen remains as mysterious as ever and, it is hoped, to be elucidated by further research. Splenectomy is at present the only available

3. Patients with secondary amegakaryocytic thrombocytopenia who receive multiple transfusions of platelet-rich blood or plasma or of isolated platelets will in time exhibit a progressively shorter platelet survival time and less and less pronounced beneficial effect of the transfusion on the bleeding (Hirsch and Gardner 1952, Stefanini et al. 1952d). The mechanism of the development of resistance to platelet transfusions resides apparently in the elaboration of platelet agglutinins of increasing titre (Stefanini et al. 1952d) in the plasma of these repeatedly transfused patients.

4. Chemicals may produce thrombocytopenia by different mechanisms. Some (aminopterin, tri-ethylene-melamine, chloramphenicol, &c.) cause aplasia of the megakaryocytes either after prolonged administration or, in especially hypersensitive people, after the administration of even a single dose. Others (quinidine, sedormid, and, possibly, arsenicals) destroy platelets in the circulation and inhibit activity of megakaryocytes in sensitised individuals.

TABLE II—COMPARATIVE CLASSIFICATION OF I.T.P. AND HÆMOLYTIC ANÆMIA

—	Idiopathic thrombocytopenic purpura	Hæmolytic anæmia
Intrinsic abnormality	Hereditary: 1, Thrombocytopathic thrombocytopenic purpura; 2, Thrombo-asthenia	Spherocytosis; Leptocytosis; Drepanocytosis; Others
	Acquired: Thrombocytopathic thrombocytopenic purpura	1, Pernicious anæmia; 2, Paroxysmal nocturnal hæmoglobinuria
Extrinsic disturbance	Bacterial or viral (?)	Bacterial or viral (bartonella, streptococcus, &c.)
		Chemical
	Auto-immune*: "idiopathic"; "symptomatic"	Auto-immune: "idiopathic"; "symptomatic"
	Hypersplenic	Hypersplenic

Combined types
Auto-immune thrombocytopenia with hæmolytic anæmia
Thrombotic thrombocytopenic purpura

* Possibly allergic in "acute I.T.P."; immunological (antibodies) in "chronic I.T.P."

treatment for chronic I.T.P. and is completely successful in about 60% of cases. The success of splenectomy does not appear related to the presence of demonstrable agglutinins, unless these are present in very high concentration. In this case splenectomy is likely to induce but a temporary beneficial result. It is the recommended procedure in the relatively mild cases because of the real danger of relapse or of hæmorrhagic crisis. This may occur impredictably and place the patient's life in jeopardy. To be sure, it is impossible to guarantee the results of splenectomy in a given instance; but, since completely beneficial results follow so often, and since the risks of the operation are now so small (corticotrophin, platelet transfusions), the operation can be recommended in all conscience.

Conclusions

Our present studies and concepts may be said to be in the "groping" stage. They lean heavily on an immunological concept, although some other humoral mechanisms, perhaps emanating from the spleen, cannot be ruled out. How or why platelet antibodies (agglutinins), destructive to the patient's own platelets, are evolved is at present quite mysterious. It is known that platelets and their products are antigenic. This is demonstrated not only by the development of platelet agglutinins by laboratory animals receiving heterologous platelets, but also by the presence of anti-platelet agents in the plasma of thrombocytopenic patients receiving multiple platelet transfusions. It is conceivable, although not demonstrated, that bacterial and viral agents and other noxious factors may modify the structure of the platelet and confer on it auto-antigenic properties. It is also possible that the auto-agglutinin might be the end-result of faulty synthesis of protein by diseased organs. In any event auto-immune thrombocytopenia may be just as real as auto-immune hæmolytic anæmia. With this in mind one can therefore present a tentative classification of I.T.P. which is quite in line with the better documented one for hæmolytic anæmia (table II).

The impact of the various concepts presented here, some of them new and others highly speculative, on the ultimate understanding of the pathogenesis of I.T.P. remains to be fully assessed. An immediate result of these findings has been that of emphasising the necessity for the careful assessment of the clinical and laboratory features of each case of I.T.P., with particular reference to its acute or chronic nature. This has considerable bearing on the decision whether and, if so, when splenectomy should be done. Less practical, but theoretically very important, has been the development of the concept that each case of I.T.P., whether "acute" or "chronic," may well be an individual syndrome where many different pathogenic mechanisms may play an undetermined rôle. Today I.T.P. remains perhaps somewhat less of a mystery than in Werlhof's time but nevertheless a stimulating challenge.

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". . . Popular lore and the obscure faith underlying it, whether it is that of the hedger-and-ditcher, or of the Celtic hen-wife, or of the business man from the dormitory suburb, is, in its own peculiar way, and if left to itself, quite likely to have a truer appreciation of some of the mysteries of health and sickness than the perfunctory rationality of many an average doctor or nurse. . . . We have been brought up—and by no means only by materialists—to think, or at least to talk, of the body as a machine: as something that has to be kept in good running order, certainly, but chiefly by means of stoking up regularly with the right fuel, not overtaxing the engine, and keeping an eye on the oil-gauge. Popular superstition continues to think of the body rather as an ambulatory vegetable, a cerebrating carrot that, like any other carrot lives with the seasons, weather, quality of the land, and the nature of previous crops, as well, perhaps, as with the phases of the moon and what songs were sung at sowing time, what dances stamped out, perhaps even what blood was spilt; and in this bifurcated, wandering, and natural organism, as in its ominous little counterpart the mandrake, there is a soul. Is there less philosophic truth in the image of the animated mandrake root whose scream kills the hearer than in the image of the electronic brain?"—*Times Literary Supplement*, July 17, 1953, p. 454.

LABORATORY TECHNIQUES FOR THE DETERMINATION OF SENSITIVITY OF TUBERCLE BACILLI TO ISONIAZID, STREPTOMYCIN, AND P.A.S.

(M.R.C. Isoniazid Trial: Report No. 3)

REPORT BY THE LABORATORY SUBCOMMITTEE OF THE TUBERCULOSIS CHEMOTHERAPY TRIALS COMMITTEE, MEDICAL RESEARCH COUNCIL*

WHEN, in February, 1952, the Medical Research Council's Tuberculosis Chemotherapy Trials Committee planned its trial of isonicotinic acid hydrazide (isoniazid) in the treatment of pulmonary tuberculosis, a laboratory subcommittee was formed of bacteriologists and pathologists at the coöperating hospitals. This subcommittee laid down the laboratory techniques and procedures for the centres. Among the most important of these laboratory investigations is the determination of bacterial sensitivity to isoniazid, the method for which was outlined in the first two reports on the trial (Medical Research Council 1952, 1953a). In view of the increasing use of this drug, alone or in combination with streptomycin or *p*-aminosalicylic acid (P.A.S.), it was thought desirable to describe in greater detail the tests which have been employed for estimating bacterial sensitivity to each of the three drugs in the course of the present trial. The results so far obtained with these sensitivity tests in the trial are analysed in the fourth report (Medical Research Council 1953b).

It is not suggested that these methods are necessarily the best or most accurate, but they were devised and adopted as most suited to the resources of the coöperating laboratories.

This report was prepared by the Medical Research Council's Tuberculosis Research Unit, with the collaboration of Dr. D. A. Mitchison.

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The subcommittee wishes to emphasise the necessity for observing the greatest care in laboratory procedures connected with tubercle bacilli. Instances have occurred in the past in which the development of a tuberculous infection in a member of a laboratory staff may possibly have been related to handling specimens or cultures containing tubercle bacilli.

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Stock Solution

A 1% solution of crystalline isoniazid ('Nydrazid,' Squibb) was sterilised by filtration through a Seitz filter or Chamberland L3 candle. This solution was stable during at least 3 months' storage in the refrigerator, as judged by biological assay.

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Tests were carried out on slopes of Löwenstein-Jensen medium. A number of slight modifications of this medium were used in different laboratories. Isoniazid was added prior to inspissation, which was carried out for one hour at not more than 90°C. This amount of heating did not cause loss of activity of isoniazid in Tween-albumin medium. However, there is evidence of progressive loss of activity in Tween-albumin medium when incubated at 37°C over a period of six weeks (Knox et al. 1952, Mitchison 1952), though as yet there is no evidence on heat-inactivation of isoniazid in solid medium.

Inoculum

As soon as possible after the primary culture from the specimen had become positive, a representative loopful, obtained from all parts of the growth, was suspended in 0·3–0·5 ml. of sterile distilled water. Convenient methods were either to grind up the sample of the culture in a Griffith's tube containing the water, or to add it to a small (bijou) screw-capped bottle containing the water and a few glass beads and then to shake the bottle for two to three minutes. The final suspension was opalescent, although no attempt was made to standardise the opacity accurately. Since, however, dilution of such an inoculum by a hundredfold has been found to cause a fourfold reduction in the apparent average degree of resistance of resistant strains (Mitchison 1953), it may be advisable in future to make a more accurate adjustment of the opacity—e.g., so that it is approximately equal to that of a ten-day culture of H37Rv in Tween-albumin medium.

Technique and Recording

A 3-mm. loopful of the bacillary suspension was spread over the surface of Löwenstein-Jensen slopes containing isoniazid in concentrations of 0, 0·2, 1, 5, 10, and 50 μg. per ml. The tests were read after fourteen and twenty-eight days' incubation at 37°C. The amount of growth on each slope was recorded as "confluent growth," "innumerable discrete colonies," "20–100 colonies," the actual number of colonies when fewer than 20 grew, or "nil." Analysis of a random sample of 480 tests on both sensitive and resistant strains showed that growth on the isoniazid-free control slope after four weeks' incubation was almost always profuse; growth was confluent in 87% of the tests and there were innumerable discrete colonies in a further 10%.

Definitions of Growth, Resistance, and Sensitivity

The amount of growth on isoniazid-containing slopes, after four weeks' incubation, for 354 cultures obtained from the same number of patients before treatment, is given in table I. It will be seen that occasional colonies grew even when the concentration of isoniazid was as high as 5 or 10 μg. per ml. (though the number of colonies decreased with increasing isoniazid concentration). Such colonies also appeared in the parallel tests on the standard strain H37Rv. In no instance did 20 or more colonies appear prior to treatment on slopes containing 1 μg. per ml. or higher concentrations of isoniazid.

In view of these findings the definition of "growth" in the presence of isoniazid was taken as the appearance of 20 or more colonies, and the inhibitory end-point as the lowest concentration which prevented this "growth." In 326 of the 354 sensitivity tests (92%) the test strain showed "no growth" (i.e., less than

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TABLE II—COMPARATIVE CLASSIFICATION OF I.T.P. AND HÆMOLYTIC ANÆMIA

—	Idiopathic thrombocytopenic purpura	Hæmolytic anæmia
Intrinsic abnormality	Hereditary { 1, Thrombocytopathic thrombocytopenic purpura; 2, Thrombo-asthenia	Spherocytosis; Leptocytosis; Drepanocytosis; Others
	Acquired — Thrombocytopathic thrombocytopenic purpura	{ 1, Pernicious anæmia; 2, Paroxysmal nocturnal hæmoglobinuria
Extrinsic disturbance	Bacterial or viral (?)	Bacterial or viral (bartonella, streptococcus, &c.)
		Chemical
	Auto-immune* { "idiopathic"; "symptomatic"	Auto-immune { "idiopathic"; "symptomatic"
	Hypersplenic	Hypersplenic
Combined types	Auto-immune thrombocytopenia with hæmolytic anæmia; Thrombotic thrombocytopenic purpura	

* Possibly allergic in "acute I.T.P."; immunological (antibodies) in "chronic I.T.P."

treatment for chronic I.T.P. and is completely successful in about 60% of cases. The success of splenectomy does not appear related to the presence of demonstrable agglutinins, unless these are present in very high concentration. In this case splenectomy is likely to induce but a temporary beneficial result. It is the recommended procedure in the relatively mild cases because of the real danger of relapse or of hæmorrhagic crisis. This may occur impredictably and place the patient's life in jeopardy. To be sure, it is impossible to guarantee the results of splenectomy in a given instance; but, since completely beneficial results follow so often, and since the risks of the operation are now so small (corticotrophin, platelet transfusions), the operation can be recommended in all conscience.

Conclusions

Our present studies and concepts may be said to be in the "groping" stage. They lean heavily on an immunological concept, although some other humoral mechanisms, perhaps emanating from the spleen, cannot be ruled out. How or why platelet antibodies (agglutinins), destructive to the patient's own platelets, are evolved is at present quite mysterious. It is known that platelets and their products are antigenic. This is demonstrated not only by the development of platelet agglutinins by laboratory animals receiving heterologous platelets, but also by the presence of anti-platelet agents in the plasma of thrombocytopenic patients receiving multiple platelet transfusions. It is conceivable, although not demonstrated, that bacterial and viral agents and other noxious factors may modify the structure of the platelet and confer on it auto-antigenic properties. It is also possible that the auto-agglutinin might be the end-result of faulty synthesis of protein by diseased organs. In any event auto-immune thrombocytopenia may be just as real as auto-immune hæmolytic anæmia. With this in mind one can therefore present a tentative classification of I.T.P. which is quite in line with the better documented one for hæmolytic anæmia (table II).

The impact of the various concepts presented here, some of them new and others highly speculative, on the ultimate understanding of the pathogenesis of I.T.P. remains to be fully assessed. An immediate result of these findings has been that of emphasising the necessity for the careful assessment of the clinical and laboratory features of each case of I.T.P., with particular reference to its acute or chronic nature. This has considerable bearing on the decision whether and, if so, when splenectomy should be done. Less practical, but theoretically very important, has been the development of the concept that each case of I.T.P., whether "acute" or "chronic," may well be an individual syndrome where many different pathogenic mechanisms may play an undetermined rôle. Today I.T.P. remains perhaps somewhat less of a mystery than in Werlhof's time but nevertheless a stimulating challenge.

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"... Popular lore and the obscure faith underlying it, whether it is that of the hedger-and-ditcher, or of the Celtic hen-wife, or of the business man from the dormitory suburb, is, in its own peculiar way, and if left to itself, quite likely to have a truer appreciation of some of the mysteries of health and sickness than the perfunctory rationality of many an average doctor or nurse. ... We have been brought up—and by no means only by materialists—to think, or at least to talk, of the body as a machine: as something that has to be kept in good running order, certainly, but chiefly by means of stoking up regularly with the right fuel, not overtaxing the engine, and keeping an eye on the oil-gauge. Popular superstition continues to think of the body rather as an ambulatory vegetable, a cerebrating carrot that, like any other carrot lives with the seasons, weather, quality of the land, and the nature of previous crops, as well, perhaps, as with the phases of the moon and what songs were sung at sowing time, what dances stamped out, perhaps even what blood was spilt; and in this bifurcated, wandering, and natural organism, as in its ominous little counterpart the mandrake, there is a soul. Is there less philosophic truth in the image of the animated mandrake root whose scream kills the hearer than in the image of the electronic brain?"—*Times Literary Supplement*, July 17, 1953, p. 454.

LABORATORY TECHNIQUES FOR THE DETERMINATION OF SENSITIVITY OF TUBERCLE BACILLI TO ISONIAZID, STREPTOMYCIN, AND P.A.S.

(M.R.C. Isoniazid Trial: Report No. 3)

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The amount of growth on isoniazid-containing slopes, after four weeks' incubation, for 354 cultures obtained from the same number of patients before treatment, is given in table I. It will be seen that occasional colonies grew even when the concentration of isoniazid was as high as 5 or 10 μg. per ml. (though the number of colonies decreased with increasing isoniazid concentration). Such colonies also appeared in the parallel tests on the standard strain H37Rv. In no instance did 20 or more colonies appear prior to treatment on slopes containing 1 μg. per ml. or higher concentrations of isoniazid.

In view of these findings the definition of "growth" in the presence of isoniazid was taken as the appearance of 20 or more colonies, and the inhibitory end-point as the lowest concentration which prevented this "growth." In 326 of the 354 sensitivity tests (92%) the test strain showed "no growth" (i.e., less than

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TABLE I—AMOUNT OF GROWTH ON ISONIAZID-CONTAINING SLOPES AFTER 4 WEEKS' INCUBATION OF PRE-TREATMENT CULTURES FROM 354 PATIENTS

Number of colonies	Concentration of isoniazid (μg. per ml.)				
	0·2	1	5	10	50
None	274	338	348	62	62
1 to 4	39	11	3	1	0
5 to 9	9	3	2	0	0
10 to 19	4	2	1	0	0
20 to 100	18	0	0	0	0
Innumerable discrete colonies	8	0	0	0	0
Confluent growth	2	0	0	0	0
Total cultures	354	354	354	63	62
Percentage of cultures with 1 or more colonies	*23*	*5*	*2*	*1*	*0*

20 colonies) in any of the concentrations of isoniazid. In the remaining 28 sensitivity tests the test strain grew (20 or more colonies) on 0·2 μg. per ml. In 20 of these the parallel culture of H37Rv showed a lesser degree of growth than the test strain and in the other 8 (6 from one centre) H37Rv yielded the same or a greater degree of growth.

The following definitions of resistance and sensitivity were therefore formulated and have been applied to all cultures obtained before, during, and after treatment:

Resistant strains.—Those which grow (20 or more colonies) after four weeks' incubation on 1 μg. per ml.

Doubtfully resistant strains.—Those which grow (20 or more colonies) after four weeks' incubation on 0·2 μg. per ml., but not on 1 μg. per ml., provided that H37Rv shows a lesser degree of growth on 0·2 μg. per ml.

Sensitive strains.—Those which show no growth (i.e., less than 20 colonies) on 0·2 μg. per ml. or higher concentrations of isoniazid after four weeks' incubation; also those which grow after four weeks' incubation on 0·2 μg. per ml., but not on 1 μg. per ml., provided that H37Rv shows the same or a greater degree of growth on 0·2 μg. per ml.

There is evidence that the strains classed as "doubtfully resistant" in accordance with the above definition are sometimes sensitive and sometimes of a low degree of resistance. Thus the results of the isoniazid-sensitivity tests during treatment were analysed for the 20 patients whose pre-treatment cultures were originally classed as "doubtfully resistant." Of these patients 14 were treated with isoniazid alone (200 mg. daily) and 6 with streptomycin (1 g. daily) plus isoniazid (200 mg. daily). At the end of one month 5 patients were culture-negative and remained so subsequently; from 10 patients sensitive strains were isolated and from 2 patients (one on isoniazid, the other on streptomycin plus isoniazid) resistant strains. The remaining 3 cultures were still "doubtfully resistant"; 1 of these patients was thereafter culture-negative, and the other 2 yielded sensitive strains at two months. These findings thus suggest that a "doubtfully resistant" strain in a patient who has never received isoniazid may be regarded as sensitive. On the other hand, during treatment with isoniazid, results classed as "doubtfully resistant" occur approximately twice as frequently as they do prior to treatment, and are often followed by the appearance of a resistant strain in the same patient. Thus it is evident that a "doubtfully resistant" result during treatment with isoniazid frequently indicates a strain with a low degree of resistance.

Period of Incubation

As noted above, readings of isoniazid-sensitivity tests were made after two and four weeks' incubation, though the latter was taken as the definitive reading. The results of both sets of readings on all the 365 resistant strains which were isolated (at any monthly examination up to six months after starting treatment with isoniazid alone) from a total of 261 patients, are given in table II. These 365 strains were classified as resistant from the readings at four weeks, but if the readings had been made after two weeks' incubation, 7% would have been regarded as sensitive (no growth on 0·2 μg. per ml.). Even for the 147 most resistant strains—i.e., those in which growth finally occurred on 50 μg. per ml.—6% would have been considered sensitive at two weeks. Furthermore, during the second fortnight of incubation growth appeared in 2 or more higher concentrations of isoniazid in 69 tests—19% of the total. It may be concluded that although a two-week reading may yield early information when it indicates a resistant strain, the definitive reading should be the one at four weeks. Although further growth sometimes occurs if incubation is continued for more than four weeks, this period was adjudged the optimum to permit the growth of the resistant tubercle bacilli, without unduly delaying the final report.

Streptomycin Sensitivity

An essentially similar technique for testing bacterial sensitivity to streptomycin has been described previously (Medical Research Council 1948).

Stock Solution

A stock solution, usually containing 1% streptomycin, was prepared with sterile precautions from any of the commercial preparations of streptomycin, but not dihydrostreptomycin. Such a solution has been found to retain its potency during at least six months' storage in the refrigerator.

Medium

A modification of the Dubos and Davis (1946) Tween-albumin medium was used. It was prepared as follows:

Potassium dihydrogen phosphate (KH_2PO_4)	1·0 g.
Disodium hydrogen phosphate ($Na_2HPO_4.12H_2O$)	6·25 g.
Sodium citrate	1·5 g.
Magnesium sulphate ($MgSO_4.7H_2O$)	0·6 g.
Dissolve one at a time in distilled water.	
Add	
'Tween 80'* 10% solution	5 ml.
Casein hydrolysate† 20% solution	10 ml.
Distilled water to	1000 ml.

* Batches suitable for growth of tubercle bacilli are obtainable from Messrs. Honeywill & Stein Ltd., 21 St. James's Square, London, S.W.1.

† For preparation see Medical Research Council (1948).

The medium should have a pH of 7·2. It was distributed in quantities of 2·7 ml. into 5-ml. screw-capped bottles (bijou bottles) and autoclaved. A 9% solution of bovine albumin (Fraction V, Armour & Co.) was Seitz-filtered and 0·1 ml. added to each bottle.

Inoculum

A representative loopful, obtained from all parts of the growth on the primary culture, was partially emulsified in Tween-albumin medium by rubbing the loop on the side of the bijou bottle. This bottle was incubated for seven to ten days. If, as was usually the case, growth in this first subculture was granular, 0·1–0·2 ml. was transferred to a

TABLE II—COMPARISON OF ISONIAZID-SENSITIVITY READINGS AFTER 2 WEEKS' AND 4 WEEKS' INCUBATION FOR THE RESISTANT CULTURES OBTAINED FROM 261 PATIENTS DURING AND AFTER TREATMENT WITH ISONIAZID ALONE

Reading at 2 weeks	Total cultures	Reading at 4 weeks			
		Growth on 1 μg. per ml. not on 5	Growth on 5 μg. per ml. not on 10	Growth on 10 μg. per ml. not on 50	Growth on 50 μg. per ml.
No growth on 0·2 μg. per ml.	25	10	3	3	9
Growth on 0·2 μg. per ml. (not on 1)	44	29	4	4	7
Growth on 1 μg. per ml. (not on 5)	109	59	24	15	11
Growth on 5 μg. per ml. (not on 10)	45	..	25	17	3
Growth on 10 μg. per ml. (not on 50)	45	..	..	25	20
Growth on 50 μg. per ml.	97	..	..	..	97
Total cultures	365	98	56	64	147
Percentage of cultures apparently sensitive at 2 weeks	*7*	*10*	*5*	*5*	*6*

second bottle which was incubated for about ten days, when there was generally a good diffuse growth. This culture usually had an opacity about equal to Brown's opacity tube no. 2, but adjustment of the culture and the parallel culture of H37Rv to this standard opacity was rarely necessary since an 8-fold decrease in the inoculum size was found to have no effect on the end-point of the test. One drop (0·02 ml.) from a Pasteur pipette with a tip approximately 0·95 mm. in diameter was used as the inoculum.

Sensitivity Test

The stock solution of streptomycin was suitably diluted and 0·2 ml. of the dilution was added to bottles of Tween-albumin medium to make final concentrations of streptomycin of 0, 0·12, 0·25, 0·5, 1·0, and 2·0 units per ml. in each bottle. Cultures were also made on nutrient agar as a control of the purity of the culture of tubercle bacilli. After inoculation the bottles were incubated at 37°C with caps screwed tight; tests were read after ten days. When the strain was capable of growth in 2 units per ml., a further test was set up by inoculating the growth in the control bottle into a further series of bottles of Tween-albumin medium containing higher concentrations of streptomycin, generally increasing by 2-fold steps up to 1024 units per ml.

The sensitivity of the strain was recorded as the lowest concentration of streptomycin giving complete inhibition of growth after ten days' incubation. This end-point and the end-point for the standard strain put up at the same time were noted. Their relationship was expressed as a resistance ratio—e.g., where the test organism was inhibited by 1 unit per ml., and H37Rv by 0·25 unit per ml., the resistance ratio was 4.

Preparation of Medium Containing Streptomycin in Bulk

When numerous tests were done in any one of the coöperating laboratories, time was saved and the risk of contamination lowered if the Tween-albumin medium was distributed from bulk quantities of 172 ml. in 500 ml. conical flasks. The flasks were autoclaved and to each was added 6 ml. of 9% bovine albumin as well as one of the following amounts of a dilution of the stock solution of streptomycin :

Concentration of streptomycin in dilution (units per ml.)	*Amount added to flask (ml.)*	*Final concentration of streptomycin (units per ml.)*
100	3·6	2·0
100	1·8	1·0
100	0·9	0·5
10	4·5	0·25
10	2·25	0·12
0	0	0

The contents of the flasks were then distributed with sterile precautions in volumes of 3 ml. into bijou bottles. A convenient method was to use a series of " pourers " which were wrapped in ' Kraft ' paper and sterilised by autoclaving. One of these was then inserted into a flask, a strong spring clip was applied, and the flask was inverted and supported in a retort stand (see fig. 1). After distribution the bijou bottles were incubated for forty-eight hours to test their sterility. They could then be kept in the refrigerator for at least two months without deterioration.

Definitions of Resistance and Sensitivity

An analysis of the streptomycin sensitivity of 192 strains obtained before treatment in a previous investigation has already been reported (Medical Research Council 1948). In that investigation no strain had a resistance ratio as high as 8 nor a minimal inhibitory concentration of 2 or more units per ml.

In the present investigation, in which the same technique was used, all strains obtained before, during, or after treatment, in which the resistance ratio was 8 or more, were classified as " resistant," provided that the test organism grew in 0·5 unit per ml. or more; this latter proviso was introduced to make allowance for an occasional exceptionally low reading of the standard strain H37Rv (inhibition by 0·06 unit per ml.) which spuriously increased the resistance ratio to 8. When this occurred, check-tests in the reference laboratory indicated that the resistance ratios of these test strains were less than 8.

P.A.S. Sensitivity

Stock Solution

A 0·2% solution of the pure sodium salt (dihydrate) of P.A.S. was sterilised by filtration through a Chamberland L3 candle. Filtration through a candle or a collodion membrane (A.P.D. 0·74 μ) was found not to remove any appreciable quantity of P.A.S. from a solution containing 0·02%, whereas 22% was removed by Seitz-filtration. This solution was stored in the refrigerator and was used within a month of preparation since, if kept too long, discoloration of the solution occurred, indicating decomposition of the P.A.S.

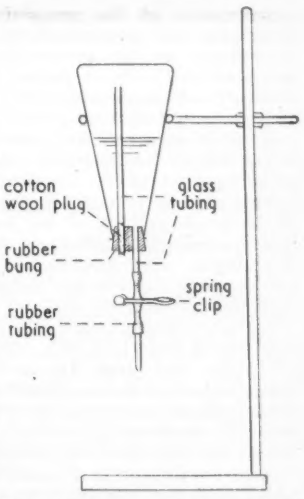

Fig. 1—Apparatus for distribution of streptomycin-containing medium, prepared in bulk, into 5-ml. bijou bottles.

Medium

Tests were carried out in Tween-albumin medium of the same composition as was used in streptomycin-sensitivity tests. It was again found preferable to add the P.A.S. to bulk volumes of the Tween-albumin medium which was then dispensed with aseptic precautions in quantities of 3 ml. into 5-ml. screw-capped bottles (bijou bottles).

Inoculum

The culture for the inoculum was prepared in the same way as for the streptomycin-sensitivity tests by subculturing the strain twice in Tween-albumin medium. The final ten-day culture had approximately the same opacity as the parallel culture of H37Rv and it was not usually necessary to adjust these to agree with a standard opacity. A 1 in 10 dilution of both cultures was then made and 0·02 ml. (1 drop from a calibrated pipette) was used as the inoculum. The importance of a small inoculum size is shown by the fact that when an inoculum of 0·02 ml. or more of the *undiluted* culture was used, growth of sensitive strains appeared in concentrations of at least 1000 μg. per ml.

Sensitivity Test

The inoculum was added to a series of bottles of Tween-albumin medium containing 0, 0·03, 0·12, 0·25, 0·5, 1·0, and 2·0 μg. per ml. of the sodium salt of P.A.S. A nutrient agar slope was also inoculated as a control of purity of the culture. The tests were set up in duplicate. When the strain was capable of growth in 2 μg. per ml., a further test was set up by inoculating the growth in the control bottle into a further series of bottles of Tween-albumin medium, containing concentrations of the sodium salt of P.A.S. increasing by 2-fold steps up to 128 μg. per ml.

The sensitivity of the strains was recorded as the lowest concentration of the sodium salt of P.A.S. giving complete inhibition of growth after fourteen days' incubation. This end-point and the end-point for the standard strain put up at the same time were noted and their relationship expressed as a resistance ratio, as for the streptomycin-sensitivity tests.

It should be noted that this test differed from the streptomycin-sensitivity test in only two details of technique. The number of tubercle bacilli in the inoculum was 10 times smaller and the definitive reading was at fourteen, not at ten, days.

Definitions of Resistance and Sensitivity

Using the technique already described, P.A.S.-sensitivity tests were carried out at the reference laboratory on 104 cultures obtained from the same number of patients before treatment. Specific inquiry elicited no history of previous P.A.S. therapy from any of these patients. The results are shown in fig. 2. The range of minimal inhibitory concentrations was from 0·03 to 1·0 μg. per ml. in 103 strains. This is a rather greater range than that found for streptomycin in an earlier series (Medical Research Council 1948). The minimal inhibitory con-

centration of the remaining strain was 8 μg. per ml; this strain, after a confirmatory test, was considered to be resistant, and has been excluded from the figure. It was presumed that the patient from whom it had been obtained had been infected with a P.A.S.-resistant strain. This patient had no history of contact.

Over the same period of time 46 tests were carried out in parallel on the standard strain H37Rv. The range of minimal inhibitory concentrations was from 0·12 to 1·0 μg. per ml. Since this range was the same as that of the great majority of the test organisms it suggests that the apparent differences in the sensitivity of the test strains were due to variations inherent in the technique, and not to real differences in the sensitivity of strains derived from different patients.

When the results were expressed as resistance ratios they ranged from 1/16 to 2, although 101 strains (98%) fell within the range 1/4 to 2. The largest number of strains had a resistance ratio of 1/2, due to the slightly lower minimal inhibitory concentrations for test strains than for the standard strain. It was presumed that test strains were less well adapted to growth in Tween-albumin medium than the standard strain, so that the inoculum of the test strain contained fewer bacteria than the inoculum of H37Rv.

Although the highest resistance ratio in this pre-treatment series was 2, occasional examples have occurred in the reference laboratory in which the resistance ratio of a strain, later proved to be sensitive by retesting, was 4, or even on one occasion 8, owing to a combination of a high reading of the test strain with a low reading of the standard strain.

From these results a strain obtained before, during, or after treatment was defined as "resistant" if the resistance ratio was 8 or more. In a few instances growth of the test strain before treatment occurred in 1 μg. per ml. but the resistance ratio was less than 8; such strains, yielding equivocal results, were not classified either as sensitive or resistant.

Discussion

In this report, the methods for testing the sensitivity of tubercle bacilli to isoniazid, streptomycin, and P.A.S., which have been adopted by the laboratories coöperating in the present Medical Research Council trial of chemotherapy in pulmonary tuberculosis, are described, and standards for sensitivity and resistance to each of the drugs are defined.

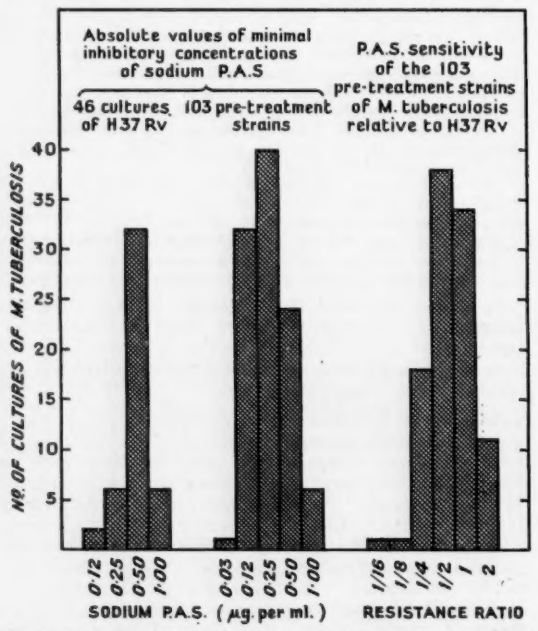

Fig. 2—P.A.S. sensitivity of pre-treatment cultures of M. tuberculosis.

In the case of isoniazid it may be assumed that none of the strains of tubercle bacilli obtained before treatment had ever come into contact with the drug previously. Among cultures examined in the coöperating laboratories "no growth" (less than 20 colonies) occurred on 0·2 μg. per ml. in 92% of 354 pre-treatment strains. The remaining 8% of tests, in which "growth" (20 or more colonies) occurred on 0·2 μg. per ml. but not on higher concentrations, probably represent variations in the technique rather than an increased resistance of a proportion of the strains. It was not possible to titrate the exact sensitivity of all strains, but, in the reference laboratory, 12 pre-treatment strains were titrated by the present method using serial 2-fold dilutions of isoniazid in Löwenstein-Jensen medium. The average minimal inhibitory concentration was 0·1 μg. per ml. with a range from 0·05 μg. per ml. to 0·2 μg. per ml.

Owing to the increasing use of streptomycin and P.A.S., there was a possibility that some patients in the present trial with no previous history of treatment might have become infected with a strain resistant to either or both of these drugs. Such an infection with a streptomycin-resistant strain appeared to have occurred in 4 out of 279 patients (Medical Research Council 1953a). The criterion of streptomycin sensitivity was therefore obtained from the results of the earlier Medical Research Council (1948) series, since at that time there was no possibility of infection with a resistant strain, and since the same method of testing has been used in the present trial.

On the other hand, prior to the present trial, there were no adequate data on the natural sensitivity of tubercle bacilli to P.A.S., using the present method of test, although, with a different technique, Karlson et al. (1949) found, at that early date, no resistant strains among 107 pre-treatment cultures. Therefore, on the assumption that naturally resistant strains, if they exist, are very rare, it was concluded that 1 patient out of a sample of 104 (1%) in the present series had been initially infected with P.A.S.-resistant organisms. This result has been excluded from the assessment of the range of natural sensitivity.

It appears therefore that the sensitivity to P.A.S. or streptomycin of strains of tubercle bacilli which have not previously come into contact with either drug was remarkably constant. The differences that occurred seemed to be due to variations inherent in the technique of measurement rather than to differences in the real sensitivities of strains.

The principle adopted in framing the definitions of resistance in this trial has been to include as resistant all strains which grew in drug-containing media to a greater extent than did any of the sensitive pre-treatment strains. A comparison between the test organism and a sensitive strain was ensured by including in each batch of tests a determination on the standard strain H37Rv. By expressing the results with streptomycin and P.A.S. as resistance ratios, allowance was made for variations in technique or medium. A defect of the method for performing isoniazid-sensitivity tests is that, although control tests on H37Rv were undertaken, it was not possible to express the results as resistance ratios owing to the limited number and uneven spacing of the drug concentrations.

The choice of methods employed for determining the sensitivity of strains presented a separate problem for each drug. In the case of isoniazid, methods involving several subcultures, especially in Tween-albumin medium, were inadvisable since Pansy et al. (1952) and Mitchison (1952) have shown that subculture may cause a consider-

able reduction in the apparent degree of resistance of resistant strains. In a United States Public Health Service (1953) investigation a method very similar to that recommended here was employed, except that egg-medium slopes containing isoniazid were inoculated from a Tween-albumin medium subculture. None of their tests on pre-treatment cultures showed growth greater than 50 colonies on 0·1 μg. per ml. or any growth in higher concentrations. The experience in the present trial was that 4% of pre-treatment strains yielded colonies on 1 μg. per ml., and colonies also appeared occasionally on higher concentrations. It is possible that in the American investigation the subculture in Tween-albumin medium may have delayed the growth of the small number of resistant organisms which produced colonies on the isoniazid-containing slopes in the present investigation. This subculture may also have caused underestimation of the degree of resistance of resistant strains.

The method of performing streptomycin-sensitivity tests is the same as that used in previous Medical Research Council trials and the results are strictly comparable. The technique has the advantages that the inoculum is standardised and the medium has a defined composition, pH, and streptomycin content. Its main disadvantages are the long time taken to obtain a reading and the possibility of contamination during subculture in liquid medium. For routine sensitivity tests the further titration of resistant strains above the 2 μg. per ml. concentration can be avoided by including bottles containing 10 and 100 μg. per ml. in the first test. The direct inoculation of sputum-concentrates on streptomycin-containing solid medium also gives a more rapid result (Holt and Cruickshank 1949, Youmans et al. 1950).

The results of P.A.S.-sensitivity tests were satisfactory only if the inoculum was small. It may well be that P.A.S. does not inhibit the growth of tubercle bacilli until after an initial period of multiplication (Sievers 1949, Desbordes 1952). This initial multiplication of the bacilli in a large inoculum might produce visible turbidity in P.A.S.-containing media (Youmans et al. 1947, Rist et al. 1951, Coletsos 1952) so that a sensitive strain would appear resistant. A large inoculum can be used in solid-medium tests without seriously affecting the inhibitory end-point (American Trudeau Society 1952, Coletsos 1952), possibly because a much larger number of divisions is required to produce visible growth on solid media than in liquid media. Provided that the inoculum is small, liquid-medium tests appear to give satisfactory results, although French and American workers have recommended solid-medium tests (Coletsos et al. 1950, American Trudeau Society 1952). Unlike streptomycin there appears to be no destruction of P.A.S. during inspissation of egg media. It is easier to make serial dilutions in liquid than in solid media, so that if a culture has already been prepared in Tween-albumin medium for inoculating streptomycin-sensitivity tests, it is probably better to carry out P.A.S.-sensitivity tests in the same medium by the method described in this report.

Even when definitions of sensitivity and resistance have been established, the clinical significance of the results of sensitivity tests is still uncertain. Although resistant strains may be present in the sputum, areas of the lungs which do not communicate with the bronchus may contain sensitive organisms (Canetti and Saenz 1951). Furthermore there may be marked fluctuations in the degree of resistance found in successive tests performed at short intervals. Finally there remains a number of strains with a low degree of resistance whose capabilities of growth in the lungs during treatment are still undecided. Nevertheless, it would be inadvisable to underestimate the possible clinical significance of a resistant result to a sensitivity test; such a result should at present be accepted as a warning that the patient may not respond to further treatment with the drug.

Summary

Laboratory techniques are described for the determination of the sensitivity of tubercle bacilli to isoniazid, streptomycin, and *p*-aminosalicylic acid (sodium salt). These techniques have been used in the coöperating laboratories during the current Medical Research Council trial of isoniazid in pulmonary tuberculosis. Definitions of bacterial sensitivity and resistance to each of the three drugs are given.

To avoid possible risk of infection of laboratory workers the subcommittee wishes to emphasise the need for great care in the performance of these and similar tests involving the handling of tubercle bacilli.

Dr. E. H. Bailey, of the Southern Group Laboratory, supplied many of the coöperating laboratories with Löwenstein-Jensen slopes containing the range of isoniazid concentrations described, and also with Tween-albumin medium. Dr. D. A. Mitchison's laboratory, at the Postgraduate Medical School of London, served as reference laboratory for drug-resistance tests. Some of the P.A.S.-sensitivity tests for the Scottish centres were undertaken by Dr. A. T. Wallace. Fig. 1 was drawn by Miss S. Treadgold, of the Department of Medical Illustration, Guy's Hospital.

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EMERGENCE OF BACTERIAL RESISTANCE IN PULMONARY TUBERCULOSIS

UNDER TREATMENT WITH ISONIAZID, STREPTOMYCIN PLUS P.A.S., AND STREPTOMYCIN PLUS ISONIAZID

(M.R.C. Isoniazid Trial: Report No. 4)

REPORT BY THE LABORATORY SUBCOMMITTEE OF THE TUBERCULOSIS CHEMOTHERAPY TRIALS COMMITTEE, MEDICAL RESEARCH COUNCIL*

IN February, 1952, the Medical Research Council appointed their Tuberculosis Chemotherapy Trials Committee to plan a clinical trial of isonicotinic acid hydrazide (isoniazid) in pulmonary tuberculosis. The trial has steadily expanded and is still continuing. The number of participating hospitals is now 53 and more than 1300 patients are undergoing or have undergone prescribed courses of treatment and observation. The present report consists of a detailed analysis of bacterial resistance, for a period of six months, for all the patients who have been treated with isoniazid alone, or with streptomycin plus *p*-aminosalicylic acid (P.A.S.), and for some of those treated with streptomycin plus isoniazid.

* The names of the members of the subcommittee are given on p. 213.

The bacteriologists and pathologists at the coöperating hospitals formed a laboratory subcommittee. This subcommittee laid down the laboratory techniques and procedures which were adopted for the examination of specimens from all trial patients (Medical Research Council 1953b). The trial was coördinated by the late Dr. Marc Daniels and by Dr. Wallace Fox, of the M.R.C. Tuberculosis Research Unit; Dr. Fox and Dr. Ian Sutherland (of the M.R.C. Statistical Research Unit) analysed the present results, and, with the collaboration of Dr. D. A. Mitchison, prepared the report. The isoniazid used throughout the trial has been supplied as 'Nydrazid' by E. R. Squibb & Sons.

Plan and Conduct of the Trial

The plan and conduct of the trial are only referred to briefly here, as they have been described in detail in the first two reports on the trial (Medical Research Council 1952, 1953a).

TYPE OF CASE

Among the basic requirements for cases admitted to the trial were the following:

At the start of treatment: (1) tubercle bacilli must have been demonstrated: there must be either a positive direct smear from a sputum specimen taken within the previous two weeks, or a positive culture derived from a specimen taken not more than two months previously. (2) The tubercle bacilli must not, so far as is known, be streptomycin-resistant or P.A.S.-resistant. (3) The patient must not have had more than 15 g. streptomycin and/or 300 g. P.A.S. within the previous three months, and not more than 3 g. isoniazid at any time (this last requirement was added soon after the start of the trial).

Cases satisfying these requirements were admitted to the trial in one of three disease groups: (1) acute rapidly progressive pulmonary tuberculosis believed to be of recent origin; (2) other forms of pulmonary tuberculosis considered suitable for chemotherapy; (3) chronic forms of pulmonary tuberculosis expected to make only a limited response to streptomycin plus P.A.S.

TREATMENT

Three treatments are studied in this report; isoniazid alone (H), streptomycin plus P.A.S. (SP), and streptomycin plus isoniazid (SH). The dosages of the drugs were:

Isoniazid.—200 mg. daily, in two doses of 100 mg. given twelve-hourly, by mouth.

Streptomycin (not dihydrostreptomycin).—1 g. daily, in one intramuscular injection.

P.A.S.—20 g. of the sodium salt daily, in four doses of 5 g., by mouth.

Treatment was allocated by the Tuberculosis Research Unit from confidentially held prearranged lists based upon random sampling numbers.

The allocation of patients to the H and SP treatments stopped on Sept. 22, 1952; the SH cases analysed in this report were also admitted before this date. Because the SH treatment was not introduced in every disease group until the trial had been running for two months, the number of SH cases available for analysis is smaller than with the other two treatments. For the same reason there was also a possibility that the SH patients might not be fully comparable with the H and SP patients. Special analyses have shown that there were no apparent differences in clinical condition on admission to the trial, nor in the development of bacterial resistance, between the H and SP cases admitted concurrently with SH cases and those admitted before the SH treatment had been introduced. It was therefore justifiable, for this study of bacterial resistance, to amalgamate the data from cases admitted to the trial in different periods.

CHEMOTHERAPY DURING THE SECOND THREE MONTHS

After admission to the trial and a preliminary week of investigation, all patients were observed for six months.

During the first three months every case received the prescribed treatment. During the second three months group-3 cases remained on the same treatment, although for SP and SH patients the dosage of streptomycin was reduced to 1 g. three times a week; for group-1 and group-2 cases the clinician was free to undertake any treatment he wished.

As a result, many different treatments have been used during the second three months. The principal régimes were the continuance of the therapy prescribed for the first three months, no further chemotherapy, or a change from one of the prescribed forms of chemotherapy to another. This diversity of treatment has reduced considerably the numbers of patients following any one clearly defined form of treatment in the second three months.

During the second three months collapse therapy was undertaken for a small number of patients in each treatment series. There is no evidence that the retention of these patients in the present bacteriological analysis has materially affected the conclusions.

TOTAL NUMBER OF PATIENTS IN THE PRESENT ANALYSIS

Isoniazid alone was allocated to a total of 289 patients, streptomycin plus P.A.S. to 283, and streptomycin plus isoniazid to 150.

Patients had to be excluded from the analysis if no results were obtained from a bacteriological examination one month after the start of treatment nor subsequently, whether the cause was discharge against medical advice (17 patients), death (3), withdrawal due to toxicity (10), or to administration of the wrong chemotherapy (3). A total of 33 patients (10 H, 18 SP, 5 SH) were so excluded. No positive pre-treatment bacteriological specimen was obtained from 25 patients (9 H, 9 SP, 7 SH), and because of this departure from the basic requirements for the trial these patients too have been excluded. An additional 34 patients (6 H, 20 SP, 8 SH) whose pre-treatment cultures were later discovered to be resistant to streptomycin or P.A.S. or both, or for whom the interpretation of either of these tests was equivocal, have been excluded from the main analysis, though some of these patients contribute to a special analysis of streptomycin resistance (table v). Three patients (3 SP), for whom no pre-treatment P.A.S.-sensitivity results were available, but who had received respectively seven, seven, and nine months of P.A.S. alone before entering the trial, were likewise excluded because it could not be assumed that their organisms were initially sensitive to that drug.

After these exclusions the numbers remaining in the main analysis were 264 H patients, 233 SP patients, and 130 SH patients.

Sensitivity Tests

Sputum collected during the pre-treatment week, and subsequently at monthly intervals, or more often, was cultured. If no sputum was produced, material from laryngeal swab or gastric lavage was cultured instead.

Strains isolated from these specimens were tested for isoniazid sensitivity in the H and SH patients and for streptomycin sensitivity in the SP and SH patients. The techniques employed are described in the third report (Medical Research Council 1953b). In addition, as the importance of initial P.A.S. resistance in patients admitted to the SP treatment became apparent, it was laid down that a P.A.S.-sensitivity test should be performed on the earliest culture available (whenever possible from the pre-treatment specimen) for all patients from whom a history of one month or more of treatment with P.A.S. alone was obtained. These tests of P.A.S. sensitivity were performed in two laboratories, and the technique was also described in the third report.

In order to assess the results as nearly as possible *at* each month after the start of treatment, a sensitivity test was accepted only if it was performed on a specimen collected not more than seven days before or after the appropriate date. When more than one such result was available, the one referring to a specimen taken on or nearest to the appropriate date was selected for analysis. Thus, in all the tables, each item represents a number of *patients* for each of whom a single test has been reported, and not a total of all the *tests* performed on a smaller number of patients. It must be remembered that an increasing proportion of bacterio-

TABLE I—RESULTS OF ISONIAZID-SENSITIVITY TESTS FOR A PERIOD OF SIX MONTHS IN PATIENTS TREATED WITH ISONIAZID ALONE (EXCLUDING THOSE FOUND TO BE STREPTOMYCIN-RESISTANT ON ENTRY TO TRIAL)

—	Months after entry to trial	Total patients with culture examined (*a*)	Culture-negative (no sensitivity test possible)	Culture-positive but no sensitivity result available	Patients culture-positive with sensitivity tests							Total resistant		
					Total results available (*b*)	Sensitive	Doubtful	Resistant						
						No growth on 0·2μg. per ml.	Growth on 0·2μg. per ml. (not on 1)	Growth on 1μg. per ml. (not on 5)	Growth on 5μg. per ml. (not on 10)	Growth on 10μg. per ml. (not on 50)	Growth on 50μg. per ml.	No. (*c*)	(*c*) as % of (*b*)	(*c*) as % of (*a*)
All patients on isoniazid alone	1	248	63	4	181	141	24	9	1	2	4	16	*9*	*6*
	2	242	91	4	147	45	30	22	12*	9	29	72	*49*	*30*
	3	243	110	1	132	27	20	22	10†	13	40	85	*64*	*35*
All patients continuing on isoniazid alone	3	73	26	1	46	9	5	8	7†	4	13	32	*70*	*44*
	4	71	29	0	42	3	6	8	8†	6	11	33	*79*	*46*
	5	57	22	2	33	2	4	6	3	3	15	27	*82*	*47*
	6	48	18	0	30	0	2	6	3†	6	13	28	*93*	*58*

* Three cultures showed growth at 5 μg. per ml. but were not tested at higher concentrations.
† One culture showed growth at 5 μg. per ml. but was not tested at higher concentrations.

logical specimens was found to be negative on culture as treatment proceeded, and consequently fewer and fewer sensitivity tests could be performed.

Emergence of Bacterial Resistance to Isoniazid

PATIENTS TREATED WITH ISONIAZID ALONE

The first part of table I sets out the results of the isoniazid-sensitivity tests on cultures obtained from patients after one, two, and three months' treatment with isoniazid alone. By three months 64% of 132 positive cultures were resistant. This figure represents 35% of the total patients on whom cultures were undertaken.

The second part of table I shows the results of isoniazid-sensitivity tests on cultures obtained after three, four, five, and six months from a smaller group of patients who continued treatment with isoniazid alone. The proportion of resistant strains recovered from this subgroup is similar at three months to the proportion in the whole group. As a consequence, the analysis from four to six months has been regarded as a continuation of that just presented up to three months. At four months 79% of 42 cultures were resistant. At five months 82% of 33 cultures were resistant. At six months 30 positive cultures were obtained from 48 patients; none was sensitive; 2 were doubtfully resistant, and 28 (93%) were resistant, 19 growing on 50 or 10 μg. of isoniazid per ml.

Summarising these results, it can be seen that on continued isoniazid treatment there was a steadily rising incidence of resistant cultures from 9% at one month to 93% at six months, when expressed as a percentage of the positive cultures. When expressed as a percentage of the total number of patients, 6% of patients yielded resistant cultures at one month and this figure steadily increased to 58% at six months.

It should also be noted that of the 33 patients who yielded resistant strains at four months, 7 did so for the first time. The corresponding figures at five months were 1 of 27 patients, and at six months 5 of 28.

PATIENTS TREATED WITH STREPTOMYCIN PLUS ISONIAZID

The development of isoniazid resistance in SH patients is in clear contrast to that just presented for H patients. Corresponding analyses are given in table II. Patients found to have streptomycin-resistant strains at the start of treatment have been excluded. By three months 11% of 28 positive cultures were resistant, and resistant strains had been isolated from 2% of all SH patients, compared with 64% and 35% respectively for H patients.

During the second three months most of the patients who continued on streptomycin plus isoniazid did so on a reduced dosage of streptomycin (1 g. three times or 1 g. twice a week). At four months 3 † of 14 positive cultures from 58 patients were resistant to isoniazid and at five months 2 †* of 8 cultures from 57 patients. At six months only 4 positive cultures were obtained and 2 of them were resistant. Strains from both of these patients had been resistant at two months. At six months, the 2 resistant strains represent 3% of the 58 patients for whom cultures were undertaken.

Emergence of Bacterial Resistance to Streptomycin

PATIENTS TREATED WITH STREPTOMYCIN PLUS P.A.S.

The first part of table III sets out the results of the streptomycin-sensitivity tests on cultures obtained from patients after one, two, and three months' treatment with streptomycin 1 g. daily plus P.A.S. (sodium salt) 20 g. daily. Patients found at the start of treatment to have

† Including 1 patient for whom this was the first resistant strain isolated.

TABLE II—RESULTS OF ISONIAZID-SENSITIVITY TESTS FOR A PERIOD OF SIX MONTHS IN PATIENTS TREATED WITH STREPTOMYCIN PLUS ISONIAZID (EXCLUDING THOSE FOUND TO BE STREPTOMYCIN-RESISTANT ON ENTRY TO TRIAL)

—	Months after entry to trial	Total patients with culture examined (*a*)	Culture-negative (no sensitivity test possible)	Culture-positive but no sensitivity result available	Patients culture-positive with sensitivity tests							Total resistant		
					Total results available (*b*)	Sensitive	Doubtful	Resistant						
						No growth on 0·2μg. per ml.	Growth on 0·2μg. per ml. (not on 1)	Growth on 1μg. per ml. (not on 5)	Growth on 5μg. per ml. (not on 10)	Growth on 10μg. per ml. (not on 50)	Growth on 50μg. per ml.	No. (*c*)	(*c*) as % of (*b*)	(*c*) as % of (*a*)
All patients on streptomycin plus isoniazid	1	123	44	2	77	68	6	3	0	0	0	3	*4*	*2*
	2	122	66	0	56	48	3	5	0	0	0	5	*9*	*4*
	3	120	91	1	28	24	1	1	1	0	1	3	*11*	*2*
All patients continuing on streptomycin plus isoniazid	3	65	49	1	15	14	0	0	1	0	0	1	*(7)*	*2*
	4	58	43	1	14	10	1	0	1	1	1	3	*(21)*	*5*
	5	57	48	1	8	6	0	1	1	0	0	2	*(25)*	*4*
	6	58	54	0	4	2	0	1	1	0	0	2	*(50)*	*3*

Percentages based upon fewer than 25 observations are enclosed in parentheses, as an indication of the small totals.

TABLE III—RESULTS OF STREPTOMYCIN-SENSITIVITY TESTS FOR A PERIOD OF SIX MONTHS IN PATIENTS TREATED WITH STREPTOMYCIN PLUS P.A.S. (EXCLUDING THOSE FOUND TO BE RESISTANT TO STREPTOMYCIN OR P.A.S. ON ENTRY TO TRIAL)

—	Months after entry to trial	Total patients with culture examined (*a*)	Culture-negative (no sensitivity test possible)	Culture-positive but no sensitivity result available	Patients culture-positive with sensitivity tests				Total resistant		
					Total results available (*b*)	Sensitive	Moderately resistant (ratio 8 to 99)	Strongly resistant (ratio 100 or more)	No. (*c*)	(*c*) as % of (*b*)	(*c*) as % of (*a*)
All patients on streptomycin plus P.A.S.	1	215	78	6	131	130	1	0	1	*1*	*0*
	2	219	122	6	91	91	0	0	0	*0*	*0*
	3	219	147	4	68	64	3	1	4	*6*	*2*
All patients continuing on streptomycin plus P.A.S.	3	68	51	0	17	16	0	1	1	*(6)*	*1*
	4	62	51	1	10	8	0	2	2	*(20)*	*3*
	5	54	42	2	10	7	2	1	3	*(30)*	*5*
	6	44	36	1	7	5	1	1	2	*(29)*	*5*

Percentages based upon fewer than 25 observations are enclosed in parentheses, as an indication of the small totals.

organisms resistant to streptomycin or P.A.S. have been excluded. At three months 219 patients yielded 68 cultures on which sensitivity tests were performed; 4 were resistant, 3 moderately and 1 strongly. Thus 6% of cultures were resistant, representing 2% of the total number of patients.

The second part of table III shows the results of streptomycin-sensitivity tests on cultures obtained after three, four, five, and six months from a smaller number of these patients who continued to receive streptomycin plus P.A.S. Again the proportion of resistant strains isolated from this subgroup is closely similar at three months to the proportion in the whole group. The dosage of streptomycin after the third month was usually 1 g. three times a week, but in a few cases 1 g. twice a week; a minority continued on daily streptomycin. All the patients continued with daily P.A.S., in a few cases also on a reduced dosage. At four months, out of 10 patients with cultures tested, 2 † yielded resistant strains. At five months, 3 ‡ out of 10 patients had resistant strains and at six months 2 † out of 7 patients. If these resistant strains are expressed as a percentage of the total cultures undertaken, the figures are 3%, 5%, and 5% at four, five and six months respectively. Because the number of cultures available for test is small it is uncertain whether there was a real increase in the percentage of resistant strains during this period. The small numbers also prevented a comparison between the effects of intermittent and continuous streptomycin therapy.

PATIENTS TREATED WITH STREPTOMYCIN PLUS ISONIAZID

Table IV presents the results of streptomycin-sensitivity tests in SH patients. By three months 26 positive cultures from 120 patients yielded 2 resistant strains. These strains represent 8% of the positive cultures, and 2% of all the patients for whom cultures were undertaken. The corresponding figures for SP patients were 6% and 2%.

After the third month, those who continued on streptomycin plus isoniazid usually received only 3 g. or 2 g. streptomycin per week. At four months no resistant strains were found in 14 positive cultures from 58 patients; at five months 1 of 8 positive cultures was resistant (resistance ratio 8). At six months 4 positive cultures were obtained from 58 patients; all were sensitive to streptomycin. The patient from whom moderately resistant strains were obtained at three and five months yielded sensitive strains at four and six months; this patient had consistently yielded strains resistant to *isoniazid* from two months onwards.

Nevertheless, owing to the small numbers of strains resistant either to streptomycin or to isoniazid, isolated at any time from SH patients, it has not been possible to determine whether, when the bacilli of a patient on this treatment become resistant to one of the drugs, they usually become resistant to the other as well.

SIGNIFICANCE OF INITIAL P.A.S. RESISTANCE IN PATIENTS TREATED WITH STREPTOMYCIN PLUS P.A.S.

In the second report (Medical Research Council 1953a) a brief reference was made to the emergence of streptomycin resistance in patients treated with streptomycin plus P.A.S. who gave a previous history of administration of P.A.S. alone.

An analysis of all the available material from the present trial has now been made. It demonstrates that the emergence of streptomycin resistance is closely associated with the sensitivity or resistance of organisms to P.A.S. when treatment with streptomycin plus P.A.S. is started.

As a result of special inquiries into P.A.S. sensitivity on entry to the trial, mainly in patients who had received this drug alone previously, two small but sharply contrasted groups of patients have been identified. Pre-treatment cultures from 12 patients were found to be

‡ Including 2 patients for whom this was the first resistant strain isolated.

TABLE IV—RESULTS OF STREPTOMYCIN-SENSITIVITY TESTS FOR A PERIOD OF SIX MONTHS IN PATIENTS TREATED WITH STREPTOMYCIN PLUS ISONIAZID (EXCLUDING THOSE FOUND TO BE STREPTOMYCIN-RESISTANT ON ENTRY TO TRIAL)

—	Months after entry to trial	Total patients with culture examined (*a*)	Culture-negative (no sensitivity test possible)	Culture-positive but no sensitivity result available	Patients culture-positive with sensitivity tests				Total resistant		
					Total results available (*b*)	Sensitive	Moderately resistant (ratio 8 to 99)	Strongly resistant (ratio 100 or more)	No. (*c*)	(*c*) as % of (*b*)	(*c*) as % of (*a*)
All patients on streptomycin plus isoniazid	1	123	44	3	76	75	1	0	1	*1*	*1*
	2	122	66	1	55	53	1	1	2	*4*	*2*
	3	120	91	3	26	24	2	0	2	*8*	*2*
All patients continuing on streptomycin plus isoniazid	3	65	49	2	14	13	1	0	1	*(7)*	*2*
	4	58	43	1	14	14	0	0	0	*(0)*	*0*
	5	57	48	1	8	7	1	0	1	*(12)*	*2*
	6	58	54	0	4	4	0	0	0	*(0)*	*0*

Percentages based upon fewer than 25 observations are enclosed in parentheses, as an indication of the small totals.

TABLE V—RESULTS OF STREPTOMYCIN-SENSITIVITY TESTS IN SP PATIENTS WITH STRAINS INITIALLY STREPTOMYCIN-SENSITIVE AND P.A.S.-SENSITIVE, AND IN SP PATIENTS WITH STRAINS INITIALLY STREPTOMYCIN-SENSITIVE AND P.A.S.-RESISTANT

P.A.S. sensitivity on entry to trial	Months after entry to trial	Total patients with culture examined (*a*)	Culture-negative (no sensitivity test possible)	Culture-positive but no sensitivity result available	Patients culture-positive with sensitivity tests				Total resistant		
					Total results available (*b*)	Sensitive	Moderately resistant (ratio 8 to 99)	Strongly resistant (ratio 100 or more)	No. (*c*)	(*c*) as % of (*b*)	(*c*) as % of (*a*)
Sensitive	1	12	6	0	6	6	0	0	0	(*0*)	(*0*)
	2	12	8	0	4	4	0	0	0	(*0*)	(*0*)
	3	11	7	0	4	3	1	0	1	(*25*)	(*9*)
Resistant	1	10	2	0	8	8	0	0	0	(*0*)	(*0*)
	2	9	2	0	7	2	3	2	5	(*71*)	(*56*)
	3	10	2	0	8	1	4	3	7	(*88*)	(*70*)

Percentages based upon fewer than 25 observations are enclosed in parentheses, as an indication of the small totals.

sensitive both to streptomycin and to P.A.S.; all these patients had received P.A.S alone, for periods varying from one to fourteen months, before entering the trial. Pre-treatment cultures from another 10 patients were found to be sensitive to streptomycin but resistant to P.A.S.; 9 of these patients had received P.A.S. alone, for periods varying from two to seven months, before entering the trial; the other patient gave no history of previous P.A.S. therapy. The development of streptomycin resistance at one, two, and three months in these two groups has been analysed in table V.

At three months 8 of the 10 patients whose organisms were initially P.A.S.-resistant yielded positive cultures; 7 of the cultures were streptomycin-resistant (3 being strongly resistant) and only 1 was sensitive. In contrast, 11 of the 12 patients whose organisms were initially P.A.S.-sensitive yielded 4 cultures, only 1 of which was streptomycin-resistant (ratio 32). The twelfth patient in this group had died. The analysis could not be taken further than three months because of the variety of treatments which were introduced at the end of this period.

These results indicate that over a three-month period streptomycin resistance in patients treated with streptomycin plus P.A.S. occurs more often in those who had P.A.S.-resistant strains initially than in those who had P.A.S.-sensitive strains.

Four more SP patients who had received P.A.S. alone before entering the trial were not included in the above analysis because no streptomycin- or P.A.S.-sensitivity results were obtained from pre-treatment cultures. The first available cultures from all 4 were found to be sensitive both to streptomycin and to P.A.S.—2 at four months and 2 at five months. It is hard to believe that strains initially resistant to either drug could have become sensitive to both while the patients were receiving the combined treatment. It is therefore highly probable that the bacilli from these patients were sensitive to both drugs on entry to the trial, and so it is arguable that these 4 cases might have been included in the group of patients with organisms initially sensitive to P.A.S., thereby intensifying the contrast with the other group.

Incidence of Bacterial Resistance after Cessation of Treatment with Isoniazid

Analyses of isoniazid resistance were made at three, four, five, and six months on the H patients for whom chemotherapy was stopped at three months, and also on those who were given chemotherapy which did not include isoniazid during the second three months. As regards isoniazid resistance the behaviour of these two groups was the same. The results have therefore been amalgamated in table VI in order to study isoniazid resistance for a three-month period after the cessation of treatment with isoniazid. At three months the proportion of resistant strains in this subgroup (table VI) tallies closely with that of the whole group (table I). At four months 58 positive cultures were obtained from 135 patients; of these 66% were resistant. The corresponding proportions were 80% at five months and 67% at six months. This analysis offers no evidence of reversion to sensitivity.

The question of possible reversion of the resistance of strains from individual H patients either to a lower level of resistance or to sensitivity after the cessation of isoniazid therapy is considered in more detail in table VII. This table gives the results of all pairs of sensitivity tests carried out on strains isolated at three and six months from the same patient. Of 28 patients with resistant strains at three months, 1 yielded a sensitive strain at six months, and 2 others doubtfully resistant strains. On the other hand, resistant strains were isolated at six months from 3 of 7 patients who yielded sensitive or doubtfully resistant organisms at three months. Moreover, for the entire group, the results of the two sensitivity tests were similar for strains from 80% of patients; the

TABLE VI—RESULTS OF ISONIAZID-SENSITIVITY TESTS FOR A PERIOD OF THREE MONTHS AFTER TREATMENT WITH ISONIAZID HAD STOPPED IN PATIENTS ALREADY TREATED FOR THREE MONTHS WITH ISONIAZID ALONE

—	Months after entry to trial	Total patients with culture examined (*a*)	Culture-negative (no sensitivity test possible)	Culture-positive but no sensitivity result available	Patients culture-positive with sensitivity tests							Total resistant		
					Total results available (*b*)	Sensitive	Doubtful	Resistant				No. (*c*)	(*c*) as % of (*b*)	(*c*) as % of (*a*)
						No growth on 0·2 μg. per ml.	Growth on 0·2 μg. per ml. (not on 1)	Growth on 1 μg. per ml. (not on 5)	Growth on 5 μg. per ml. (not on 10)	Growth on 10 μg. per ml. (not on 50)	Growth on 50 μg. per ml.			
All H patients receiving no chemotherapy, or chemotherapy not including isoniazid, during the second three months	3	154	81	0	73	13	11	7	8	8	26	49	*67*	*32*
	4	135	73	4	58	9	11	9	7	11	11	38	*66*	*28*
	5	131	72	5	54	6	5	7	11	8	17	43	*80*	*33*
	6	127	76	3	48	9	7	7	5	12*	8	32	*67*	*25*

* One culture showed growth at 10 μg. per ml. but was not tested at 50 μg. per ml.

TABLE VII—RESULTS OF ISONIAZID-SENSITIVITY TESTS AT THREE AND AT SIX MONTHS AFTER ENTRY TO TRIAL IN PATIENTS TREATED FOR THREE MONTHS WITH ISONIAZID ALONE, AND WHO RECEIVED NO ISONIAZID BETWEEN THE TWO TESTS

Result of test at three months		Total results available	Result of test at six months					
			Sensitive	Doubtful	Resistant			
			No growth on 0·2 μg. per ml.	Growth on 0·2 μg. per ml. (not on 1)	Growth on 1 μg. per ml. (not on 5)	Growth on 5 μg. per ml. (not on 10)	Growth on 10 μg. per ml. (not on 50)	Growth on 50 μg. per ml.
Sensitive	No growth on 0·2 μg. per ml. ..	4	2	0	0	1	0	1
Doubtful	Growth on 0·2 μg. per ml. (not on 1) ..	3	0	2	0	0	1	0
Resistant	Growth on 1 μg. per ml. (not on 5) ..	8	0	1	4	2	0	1
	Growth on 5 μg. per ml. (not on 10) ..	2	0	1	0	1	0	0
	Growth on 10 μg. per ml. (not on 50) ..	6	0	0	0	1	4	1
	Growth on 50 μg. per ml.	12	1	0	1	0	5	5
Total results available		35	3	4	5	5	10	8

strains from 9% became less resistant (a decrease of 2 or more concentrations of isoniazid in the sensitivity test) and from 11% more resistant (an increase of 2 or more concentrations).

In summary, over a three-month period after treatment with isoniazid had been stopped, there was no evidence of any general reversion either to a lower level of isoniazid resistance or to sensitivity, nor evidence of any general increase in the proportion of resistant strains.

Discussion

The present report studies the emergence of bacterial resistance for a period of six months in over 600 patients under three treatments, isoniazid alone (H), streptomycin plus P.A.S. (SP), and streptomycin plus isoniazid (SH). The results have been presented in two ways. The resistant cultures have been expressed as a percentage of the positive cultures on which sensitivity tests were performed, and also as a percentage of the total patients for whom cultures were undertaken, i.e., the culture-positive and culture-negative patients combined. It is likely that a proportion of the culture-negative patients are nevertheless harbouring resistant bacilli which may later reappear in the sputum. Hence a true measure of the incidence of resistance probably lies somewhere between these two percentages.

Bacterial resistance to isoniazid, when given alone, developed rapidly; at three months 64% of positive cultures (35% of all patients) yielded resistant strains; at six months the corresponding figures were 93% and 58%. However, when streptomycin was combined with isoniazid, the development of isoniazid resistance was largely prevented in patients who had streptomycin-sensitive strains when the chemotherapy was started. At three months only 11% of positive cultures were resistant, and the resistant cultures represented 2% of the total cultures undertaken. At four, five, and six months the proportions of resistant strains isolated were higher, though not nearly so high as with isoniazid alone.

There is a difference from two months onwards between these findings and those in the preliminary report of the United States Public Health Service (1953). In the latter investigation streptomycin 1 g. twice a week plus isoniazid 150 mg. to 300 mg. daily was given, and results have been published for 50 patients on this régime. At eight, twelve, sixteen, twenty, twenty-four, and twenty-eight weeks the percentages of positive cultures that were resistant to 1 μg. per ml. or more of isoniazid were 15, 21, 43, 73, 60, and 67. The corresponding percentages for the present series at two, three, four, five, and six months were not so high, being 9, 11, 21, 25, and 50, although little reliance can be placed upon the last two percentages. It is likely that two main factors contribute to the apparently less satisfactory results in the U.S. Public Health Service investigation. First, their analysis includes patients whose organisms were initially streptomycin-resistant as well as those with streptomycin-sensitive strains; the present study excludes patients with initially streptomycin-resistant organisms. Secondly, the smaller dosage of streptomycin used throughout the period in the American investigation may have been insufficient to prevent the emergence of isoniazid resistance, with the dosage of isoniazid used. (Although there are also certain differences in the technique and interpretation of isoniazid-sensitivity tests, it may be noted that the proportions of strains, classified as resistant to 1 μg. per ml. or more of isoniazid, isolated from patients given this drug alone are similar in the two investigations.) Pitts et al. (1953) using streptomycin 2 g. every third day plus isoniazid 150 mg. daily—a régime which approximates more nearly to that studied in the present trial—have reported bacteriological findings on 49 patients at a hundred and twenty days; only 2 yielded positive cultures and these were sensitive both to isoniazid and to streptomycin.

For patients treated with streptomycin plus isoniazid it is also important to know whether the combined therapy hinders the emergence of bacilli resistant to streptomycin. The present analysis has shown that this is so. At three months 8% of positive cultures were resistant, and the resistant cultures represented 2% of the 120 patients for whom cultures were undertaken. At four months 14 cultures were tested and all were sensitive; at five months 1 of 8 cultures was resistant; at six months 4 cultures from 58 patients were tested and all were sensitive. Although the numbers of positive cultures are small the present analysis suggests that the combination streptomycin plus isoniazid has a considerable effect, at least as good as that of streptomycin plus P.A.S., over a six-month period, in preventing the emergence of streptomycin resistance, in addition to a definite, though lesser, effect upon the development of isoniazid resistance.

There is in-vitro evidence (Pansy et al. 1952, Barnett et al. 1953) that strains resistant to isoniazid may revert to sensitivity when contact with isoniazid ceases, and its occurrence has been reported in patients after treatment with isoniazid is stopped (Nitti 1952, Knox 1953, Nigoghossian 1953). The present analysis provides no evidence that general reversion to sensitivity occurs over a three-month period after stopping isoniazid, and so it suggests that bacterial resistance to isoniazid is not usually transient.

The present trial has afforded an opportunity of studying the emergence of bacterial resistance to streptomycin in a large number of patients treated with streptomycin 1 g. daily plus P.A.S. 20 g. daily. In contrast to previous Medical Research Council trials of chemotherapy,

several types of pulmonary tuberculosis were studied, and the findings are thus of wide application. In patients whose organisms are sensitive both to streptomycin and to P.A.S. at the start of treatment, the development of bacterial resistance to streptomycin is to a large extent prevented by three months of this treatment; only 6% of the positive cultures (2% of the 219 patients for whom cultures were undertaken) yielded resistant strains. When a reduced dosage of streptomycin was given after the first three months (1 g. two or three times a week), the proportion of positive cultures which were found to be resistant increased to 29% at six months, though the proportion of patients from whom resistant strains were isolated was low, being 5%. Again the experience of the United States Public Health Service (1953) investigation is considerably less satisfactory, and their report finds that intermittent streptomycin plus daily P.A.S. for a period of 28 weeks is not effective in preventing the eventual emergence of streptomycin-resistant strains where cultures have been obtained. In the absence of information on P.A.S. sensitivity at the start of treatment it is hard to assess the validity of this finding.

A special analysis in the present report has shown that streptomycin resistance under treatment with streptomycin plus P.A.S. emerges much more frequently in patients whose organisms are resistant to P.A.S. at the start of treatment. Of 10 such patients, 7 yielded streptomycin-resistant organisms at three months. It is clearly essential, when studying the emergence of streptomycin resistance in patients under treatment with streptomycin plus P.A.S., to know the P.A.S. sensitivity of the pre-treatment strains. The finding also underlines the risks which are taken if a course of P.A.S. alone is prescribed for a patient. It is known that P.A.S.-resistant strains emerge frequently in patients under this treatment (Medical Research Council 1950, Carstensen 1950, Tempel et al. 1951). It has been established in this trial that, if P.A.S. resistance develops and persists, this seriously jeopardises the efficacy of treatment with streptomycin plus P.A.S., if this is required at a later date.

Summary

As part of a clinical trial of isoniazid (isonicotinic acid hydrazide) in the treatment of pulmonary tuberculosis, the development of bacterial resistance over a period of six months to isoniazid and to streptomycin was studied in three groups of patients—264 treated with isoniazid alone, 233 with streptomycin plus P.A.S., and 130 with streptomycin plus isoniazid. The standard dosages of the three drugs were: isoniazid 100 mg. twice a day; streptomycin 1 g. daily; and P.A.S. (sodium salt) 5 g. four times a day. After three months' treatment only a proportion of patients continued with the original chemotherapy; for those who continued, the dosage of streptomycin was usually reduced to 1 g. three times or twice a week.

Treatment was determined by random allocation and the clinical condition on admission of the three treatment series was comparable.

Bacillary resistance to isoniazid was found in 64% of culture-positive patients on isoniazid alone at three months, and in 93% (28 of 30) at six months. These 28 resistant strains represent 58% of the total patients for whom cultures were undertaken. For patients on streptomycin plus isoniazid 11% of positive cultures were resistant at three months and 50% (2 of 4) at six months. These 2 resistant strains were obtained from a total of 58 patients for whom cultures were undertaken (3%).

Over a three-month period after stopping treatment with isoniazid there was no evidence of any general reversion of isoniazid-resistant strains either to a lower level of resistance or to sensitivity.

For a period of six months, streptomycin plus isoniazid was quite as effective as streptomycin plus P.A.S. in preventing the emergence of strains resistant to streptomycin. On streptomycin plus isoniazid 8% of positive cultures were streptomycin-resistant at three months and 0% (0 of 4) at six months; on streptomycin plus P.A.S. the corresponding figures were 6% and 29% (2 of 7).

Patients with organisms initially P.A.S.-resistant were not protected from the risk of development of streptomycin resistance by treatment with streptomycin plus P.A.S.

The names of members of the Laboratory Subcommittee and acknowledgments are given in the preceding report (Medical Research Council 1953b). The hospitals and doctors coöperating in the phase of the trial reported here are substantially the same as those named in the second report (Medical Research Council 1953a). The Laboratory Subcommittee expresses its thanks to the many laboratory technicians who have done detailed and valuable work for the trial.

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THE NATURE AND TREATMENT OF THE CŒLIAC-PLEXUS REFLEX IN MAN

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SUDDEN falls in blood-pressure during operations are of grave concern to surgeon and anæsthetist alike. Attention to the cœliac-plexus reflex and to the fall in blood-pressure which is its chief manifestation was first drawn by Burstein and Rovenstine (1937). The exact nature of the reflex has remained largely obscure; but I shall endeavour to show that its circulatory effects are due to a fall in cardiac output resulting from an increase in cardiac vagal tone, and that therefore the logical treatment is intravenous injection of atropine.

Burstein and Rovenstine (1938) stated that the reflex was observed in patients whose upper abdominal viscera were being handled during an operation, and that its chief sign was either the sudden disappearance of the blood-pressure readings or the localisation of the blood-pressure by a single beat at about the level of the previous diastolic pressure recording. The pulse often remained palpable at the wrist, and its rate did not change greatly. When the surgeon ceased to handle the viscera, the blood-pressure readings returned to about their former level. In the three cases reported by Burstein and Rovenstine, premedication was with morphine and either hyoscine or atropine. Anæsthesia was induced with gas, oxygen, and ether, and abdominal relaxation remained poor despite repeated additions of ether. The reflex was precipitated by "breaking" the table and by heavy pressure on deep retractors.

Experiments on dogs led Burstein to suggest that the reflex was predisposed to by a sympatheticotonic state produced by a combination of premedication with atropine and the use of ether as the anæsthetic. This state was counteracted with physostigmine, which could

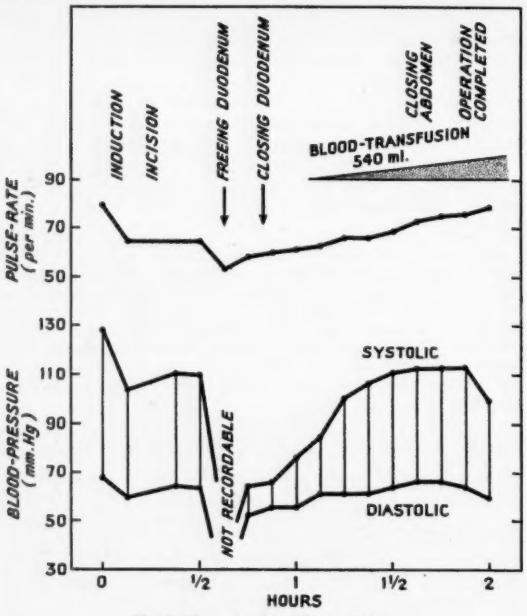

Fig. 1—Severe cœliac-plexus reflex.

The patient, aged 45, was undergoing partial gastrectomy for gastric ulcer. Omnopon gr. $^1/_3$ and hyoscine gr. $^1/_{150}$ were given one and a half hours before operation. Anæsthesia was induced with thiopentone 0·75 g. and maintained with closed-circuit gas, oxygen, and ether. Patient received altogether 41 mg. of *d*-tubocurarine chloride throughout the operation. Blood-pressure could not be recorded while duodenum was being mobilised and divided, and pulse-rate at this time was slow.

both prevent the reflex from developing and abolish it when established.

Present Series

I have observed this reflex on ten occasions. A typical blood-pressure and pulse-rate chart of an untreated case is shown in fig. 1.

The ages of the patients ranged from 26 to 68. Seven of them received premedication with 'Omnopon' gr. $^1/_3$ and hyoscine gr. $^1/_{150}$, and the remaining three with omnopon and atropine. In one case cholecystectomy was performed, in another cholecystoduodenostomy, and in the remaining eight partial gastrectomy.

In every case anæsthesia was induced with small doses of thiopentone; enough *d*-tubocurarine chloride or gallamine triethiodide was given to provide a reasonable degree of abdominal muscular relaxation, and the patients were intubated. A closed-circuit carbon-dioxide-absorption machine was used in all the cases, and respiration was either assisted or controlled. Anæsthesia was maintained with gas, oxygen, and ether in four cases, with oxygen and cyclopropane in three, and with gas and oxygen supplemented by intravenous pethidine in three.

The severity and duration of the reflex in untreated cases varied. In a severe case the blood-pressure readings disappeared completely for a short while, and the pulse pressure subsequently remained at about 8 mm. Hg for ten minutes. The blood-pressure then slowly returned during the next twenty minutes to its previous level. A less severe and more transient case is shown in fig. 2.

The strong impression emerges from experience of these cases that the cœliac-plexus reflex occurs more easily and frequently and lasts longer with a greater fall in blood-pressure, in lightly anæsthetised patients. The systolic blood-pressure has usually fallen until the pulse-pressure was about 10 mm. Hg but the Korotkov sounds have not disappeared completely. As a rule there has been a simultaneous slight fall in diastolic pressure also. The pulse-rate has slowed slightly or remained constant, but in one case it increased.

Poor relaxation and straining have not been features of the cases, but the patients, of course, had been curarised and intubated. The observation that extension of the lumbodorsal spine by raising the gall-bladder rest may precipitate the reflex has been confirmed.

One of Burstein's patients died from cardiac failure, sixty hours after operation, and a death on the operating-table was reported by Waters and Gillespie (1944). The second patient in the present series died on the operating-table:

A man, aged 56, was to undergo partial gastrectomy for a duodenal ulcer. Before operation his blood-pressure was 150/80 mm. Hg, and his pulse-rate 65. Premedication was with omnopon gr. $^1/_3$ and hyoscine gr. $^1/_{150}$ given an hour before the operation. Anæsthesia was induced with thiopentone 0·6 g., and then tubocurarine 16 mg. was given. Intubation was then performed, and anæsthesia was maintained with closed-circuit gas, oxygen, and ether.

The blood-pressure was 122/72 mm. Hg when the first incision was made, and the first twenty minutes of the operation were uneventful. When the duodenum was being freed from the pancreas, which formed the floor of the ulcer crater, the pulse became very weak and rather slow, and the patient went pale and started to sweat. Intravenously, methylamphetamine ('Methedrine') 10 mg. was given, a blood-transfusion was set up, and anæsthesia was deepened. The patient's condition deteriorated, the pulse-rate at this time being 40. The operation was stopped, the head of the table was dropped, and artificial respiration with oxygen was given. Nikethamide was also injected intravenously.

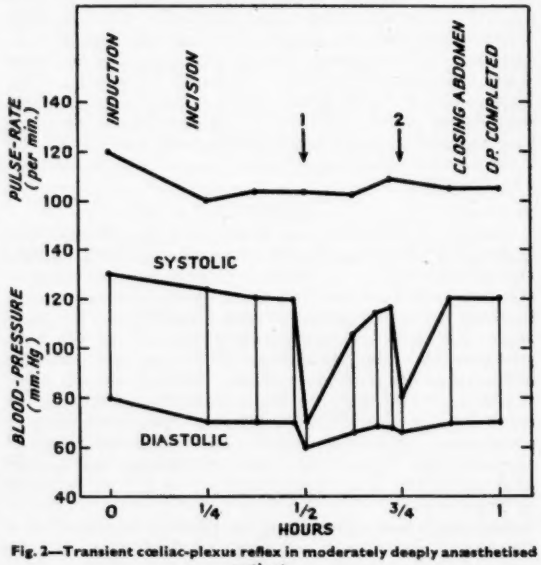

Fig. 2—Transient cœliac-plexus reflex in moderately deeply anæsthetised patient.

She was a woman aged 68, with carcinoma of head of pancreas and in poor general condition. She had been deeply jaundiced for six weeks and had secondary diabetes mellitus of recent onset, requiring twenty units of insulin daily. Omnopon gr. $^1/_6$ and atropine gr. $^1/_{100}$ were given an hour before operation, in which the gall-bladder and first part of duodenum were anastomosed. Anæsthesia was induced with thiopentone 0·35 g. and gallamine 80 mg. and maintained with cyclopropane and oxygen. At arrow 1 Korotkov sounds suddenly vanished while blood-pressure was being read and traction was exerted on stay suture through pylorus. As soon as suture was released, blood-pressure was localised at 70/60 mm. Hg. At arrow 2 blood-pressure was again greatly reduced when the tissues were under tension while anastomosis was being made.

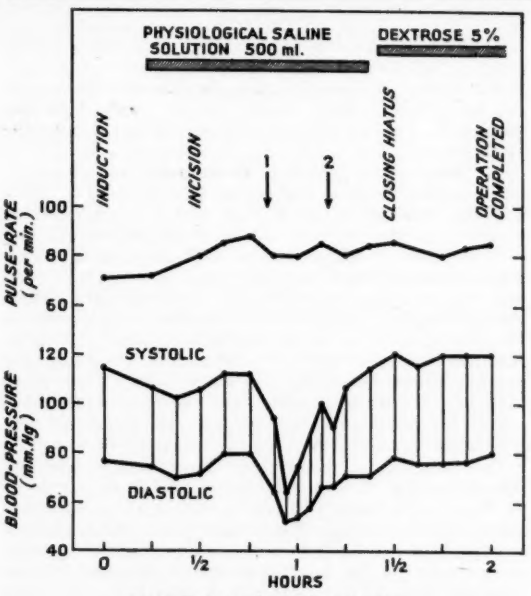

Fig. 3—Typical untreated vagal reflex.

A healthy woman, aged 51, was undergoing transabdominal repair of hiatus hernia. Omnopon gr. $^1/_3$ and hyoscine gr. $^1/_{150}$ were given one and a quarter hours before operation. Anæsthesia was induced with thiopentone 0·6 g. and maintained with gas and oxygen supplemented by a further 0·15 g. of thiopentone and pethidine 125 mg. in intermittent divided dosage. Altogether 35 mg. of tubocurarine was used to provide relaxation, and respiration was controlled throughout. At arrow 1 blood-pressure fell and pulse slowed slightly as cardia was drawn downwards. At arrow 2 further slight drop in recovering blood-pressure took place as lower end of œsophagus was being cleared.

These measures were unavailing and the patient died, cardiac massage being unsuccessful.

Necropsy showed no gross changes, though the lungs and kidneys were congested.

Mode of Production

The first descriptions of the reflex attributed it to excessive sympathetic tone, a view not disputed by Scurr (1950), though it was not certain how the fall in blood-pressure was produced. Volpitto et al. (1939) showed, with a "hypodermic manometer," that the Korotkov sounds faithfully represented the actual blood-pressure, and that the fall was not an artefact.

The systolic blood-pressure varies in fairly direct proportion to the product of the cardiac output and peripheral resistance. The fact that the diastolic pressure remains fairly constant, or falls only slightly, indicates that the peripheral resistance and the vasomotor tone are well maintained. In these cases, therefore, a fall in systolic pressure implies a decrease in cardiac output; and, as the pulse-rate remains relatively steady, this means a decrease in the output per heart beat.

Cardiac output depends on the venous return to the heart and on the force of contraction of the heart muscles. Possibly the venous return is reduced by pressure on the great veins of the abdomen by retractors or by packs, though the reflex is also met with when these are not being used. Gordh (1945), however, suggested that stimulation of the cœliac plexus might lead to loss of tone of the great veins. It is more likely that the force of contraction of the heart muscle is diminished, and that this is the primary cause of the fall in blood-pressure. Scurr (1951) reports that in some of his cases the pressure in the right auricle was high. Certainly the neck veins of patients showing this reflex are often distended. This diminished force of contraction is probably of reflex origin, for humoral or other ways in which it could be produced are difficult to imagine.

The heart is supplied by the vagus and sympathetic nerves. According to Samson Wright (1952) stimulation of the sympathetic nerves increases the rate and force of the heart beat, but stimulation of the vagus nerves produces the following effects on the heart:

(1) The heart is slowed.
(2) There is diminished force of contraction of the chambers of the heart.
(3) Conductivity of the bundle of His is impaired.
(4) The duration of systole and the refractory period are shortened.

Thus the effects of cardiac vagal stimulation are not unlike the chief manifestations of the cœliac-plexus reflex.

Moreover, blood-pressure and pulse-rate charts very similar to those obtained when the cœliac-plexus reflex occurs are sometimes obtained after surgical stimulation of the lung hilum, carotid sinus, or larynx, or after traction on the œsophagus during repair of a hiatus hernia, as in fig. 3. These are accepted as due to vagal reflexes, and Inglis (1952) points out that in these cases the blood-pressure returns to its former levels on the intravenous injection of atropine, which blocks the action of the vagus on the heart.

Diagnosis and Treatment

The diagnosis of the cœliac-plexus reflex is based on the changes in blood-pressure and pulse-rate shown on

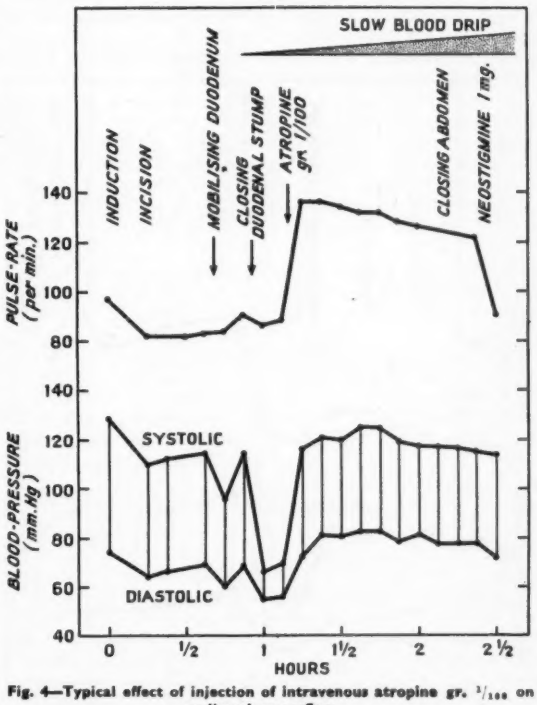

Fig. 4—Typical effect of injection of intravenous atropine gr. $^1/_{100}$ on cœliac-plexus reflex.

Blood-pressure returned to its previous levels within two minutes of injection, and pulse-rate increased simultaneously as cardiac vagal tone was decreased. Patient was a woman, aged 56, undergoing partial gastrectomy for peptic ulcer. Premedication was with omnopon gr. $^1/_3$ and hyoscine gr. $^1/_{150}$ an hour before operation. Anæsthesia, induced with thiopentone 0·5 g., was maintained with gas, oxygen, and ether, and altogether 26 mg. of *d*-tubocurarine chloride was used to provide additional abdominal relaxation.

the anæsthetist's chart, and on the condition of the patient.

Somewhat similar falls of blood-pressure may be met with in operations, most frequently cholecystectomies and operations on the common bile-duct, in which venous return from the lower half of the body is obstructed by the use of retractors or of packs, or by hyperextension of the lumbodorsal spine by a raised gall-bladder rest. In these cases the fall of blood-pressure is of slower onset and the pulse-rate increases. The cause of the trouble must be dealt with, and intravenous fluid, preferably a blood drip, must be given if necessary.

Sometimes, also, some loss of vasomotor tone is observed. Methylamphetamine may be temporarily effective; but, if the state persists, a noradrenaline drip must be set up.

The following measures should be taken as soon as the existence of the cœliac-plexus reflex is recognised:

(1) The operation should be discontinued until the situation is fully under control.
(2) The gall-bladder rest, if raised, should be lowered.
(3) An intravenous injection of atropine—sufficient to provide a fair degree of release from cardiac vagal tone—must be given immediately. Usually gr. $^1/_{100}$ should prove adequate, the dose being increased or repeated if necessary.
(4) Anæsthesia is very probably light, and should be deepened.
(5) If necessary, the surgeon can block the cœliac plexus intra-abdominally.

In cases where a slow preoperative pulse suggests a high degree of vagal tone, the following measures may be of prophylactic value:

(1) Premedication with atropine gr. $^1/_{75}$.
(2) The use of gallamine rather than *d*-tubocurarine to give abdominal relaxation.
(3) Alternatively the cœliac plexus can be blocked.

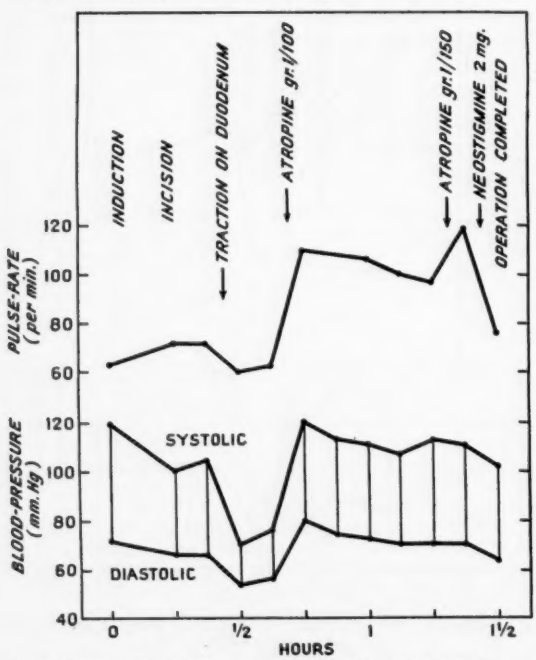

Fig. 5—Onset of cœliac-plexus reflex during manipulation of duodenum, and its rapid response to intravenous atropine.

Patient was a man, aged 37, undergoing partial gastrectomy for duodenal ulcer. He also had bronchiectasis, productive cough, and finger clubbing. An hour before operation omnopon gr. $^1/_3$ and atropine gr. $^1/_{75}$ were given. Anæsthesia was induced with thiopentone 0·5 g., and maintained with cyclopropane and oxygen, supplemented by tubocurarine 23 mg.

Discussion

The foregoing facts suggest that the cœliac-plexus reflex is not (as has been supposed) caused by sympatheticotonia: on the contrary, its principal effect—the fall in blood-pressure—is due to an increase in the vagal tone. This conclusion is supported by the following evidence.

An intravenous injection of atropine was given on six occasions when a well-marked cœliac-plexus reflex had been established, and in each case the blood-pressure returned to its previous levels or higher within two two or three minutes, and usually there was a well-marked rise within a minute. Some patients who were cold and sweating became rapidly warm and dry. There was, of course, a concomitant increase in pulse-rate to 110–130 or more as vagal tone was reduced, but in no case did this give rise to trouble, and the pulse-rate steadily decreased during the next hour as the effect of the atropine wore off. The policy now is to inject intravenous atropine gr. $^1/_{100}$ as soon as anything suggests that the cœliac-plexus reflex is about to develop (figs. 4 & 5).

The fact that in many cases the pulse-rate does not decrease much, though the cardiac effects appear to be of vagal origin, may perhaps be explained by the compensatory effects of the Bainbridge reflex. By depression of vagal tone and by sympathetic stimulation, this causes an increase in the heart-rate when increased venous pressure distends the right auricle and the great veins entering it.

It is significant that most of the patients received hyoscine as their initial premedication. This blocks the vagus less effectively than does atropine, which is used equally frequently in our cases. The normal preoperative dose of atropine or of hyoscine is insufficient to prevent vagal reflexes, for Sir Thomas Lewis (1925) pointed out that up to gr. $^1/_{10}$ of atropine was required to give complete cardiac release from vagal tone. Experience has so far shown that, when a reflex of this type occurs, intravenous atropine gr. $^1/_{100}$ gives adequate protection.

Importance is also attached to the fact that the reflex was met with only twice when gallamine, rather than *d*-tubocurarine, has been used to obtain muscular relaxation, for Doughty and Wylie (1951), among others, point out that gallamine is much the more effective in blocking the vagus.

Possibly not without significance is the fact that, though we now rarely use cyclopropane, the cœliac-plexus reflex occurred on three occasions in patients receiving it; and cyclopropane was also used in many of the cases reported in the literature. Cyclopropane was stated by Seevers et al. (1934) and by Robbins and Baxter (1937) to increase vagal tone, therein differing from chloroform and ether.

In the original report of the reflex (Burstein and Rovenstine 1937) and again later (Burstein 1949) a case was described which was treated with an injection of physostigmine 0·5 mg., after which the blood-pressure rose slowly for 40 minutes, towards its former levels, and the reflex recurred before the peritoneum was closed.

Subsequently, Burstein et al. (1949, 1950) advocated the treatment of the cœliac-plexus reflex with *d*-tubocurarine. Though this drug blocks the autonomic ganglia, it follows from the findings of Jacob and Depierre (1950) that this action would be slight when ordinary relaxant doses are used. That tubocurarine is not completely effective is shown from the fact that eight of the patients mentioned earlier in my present report had received it. Scurr (1951) believes that *d*-tubocurarine helps to prevent changes in blood-pressure associated with light anæsthesia by paralysing the muscles controlling expiratory tone, because surgical stimulation under light anæsthesia normally increases expiratory tone, decreases the thoracic cavity, and thereby interferes with cardiac filling.

Splanchnic block, effective as a measure of both prophylaxis and treatment, was advocated, among others, by Masiello and Lombardi (1949), who suggested that intravenous neostigmine, atropine, and *d*-tubocurarine might also be tried. Unfortunately, splanchnic block may lead to severe falls in blood-pressure, though McCann (1951) states that this is largely avoided if smaller quantities of more concentrated solution, placed accurately, are used.

Summary

The recorded characteristics of the cœliac-plexus reflex are reviewed, and personal observations are made of ten instances of the reflex observed in patients undergoing abdominal surgery.

The fall in blood-pressure resulting from the reflex seems to be due to vagal cardiac inhibition.

If the fall in blood-pressure is due to vagal inhibition, atropine should be an effective means of treating it. Data are presented which show the success of such treatment.

The effects of other drugs and of cœliac-plexus block on the reflex state are considered.

The diagnosis, prophylaxis, and treatment are described.

I wish to thank Dr. B. L. S. Murtagh for his advice on the management of these cases, and for his help and encouragement in the preparation of this paper.

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EFFECT OF ALKALIS ON FASTING HUMAN STOMACH

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FOR many years it has been taught that the ingestion of alkalis, particularly the soluble ones, leads to a rebound secretion of gastric juice. Like many others this statement is copied from one textbook to another without adequate consideration given to the reliability of the evidence. There is not even a clear idea of the meaning of the term: on the one hand, it is implied that after the ingestion of alkalis there is a stimulation of gastric secretion which continues after the alkali has been neutralised or has left the stomach; and on the other hand, the term is used to describe an alleged excessive secretion some hours or even days later.

There are two experimental sources of this statement: one is man, where most workers have compared the results of a fractional test-meal before and after giving alkalis without considering the volume of juice secreted; and the other is dogs with gastric pouches, where the volume of secretion from the pouches has been compared before and after the ingestion of alkalis given either alone or with food. In the light of our present knowledge on the variability of gastric secretion the human experimental results are mostly no longer tenable, and it is doubtful whether the results in dogs should be applied to man.

In the present investigation alkalis were introduced into the fasting stomach with a nonabsorbable dye, and the effect on gastric secretion was studied by taking fractional samples for two and a half hours. The experiments were not continued longer because by the end of this time a meal is normally taken, especially by those patients who are prescribed alkalis.

Methods

The patients were in hospital for the investigation and treatment of abdominal pain: 11 had a duodenal ulcer, 2 a prepyloric ulcer, and 3 pain due to other causes. A narrow-bore rubber tube with several small openings in the distal 10 cm. was passed in the early morning, and the stomach contents were aspirated. The tube was left in situ, and the stomach contents were again aspirated after an hour. Half the patients were then given 8 g. of sodium bicarbonate and 50 ml. of a solution containing 40 mg. of phenol-red per 100 ml. The other half were given 8 g. of magnesium trisilicate with 50 ml. of the phenol-red solution. Thereafter at half-hourly intervals for two and a half hours about 5 ml. of the stomach contents was aspirated.

All the specimens were next analysed for free and total acid (Töpfer's reagent and phenolphthalein as indicators), total chloride (electrometric titration), and phenol-red concentration by Hunt's (1947) method. With this method it was possible to measure the phenol-red concentration down to 0·4 mg. per 100 ml. Below this concentration it could still be detected by the naked eye though it was not measurable in the photometer. It represents a reduction in concentration to 1% compared with the solution introduced into the stomach, and it was quite adequate for the purposes of this investigation.

In addition on another day a standard histamine test was done on all the patients by the method described by Ihre (1947). After aspiration of the fasting contents 0·5 mg. of histamine acid phosphate is given by subcutaneous injection, and the gastric contents are recovered by continuous suction for an hour with a water suction apparatus set for a negative pressure of 35–40 mm. Hg. With this method Ihre found that 180 ml. represents the upper limit of normal secretion, any figure above this indicating hypersecretion.

Results

The results of the fractional analyses as regards free HCl and phenol-red concentrations are summarised in the accompanying table. The results for total acidity and total chlorides are not included, because they did not reveal any additional information. The figures for the phenol-red concentrations are given in parentheses after the free HCl concentrations, and they are recorded as a percentage reduction of the concentration of the dye on introduction. There are, of course, two factors responsible for this reduction in concentration: the diluting effect of swallowed saliva and subsequent gastric secretion, and the loss of dye through the pylorus. Unfortunately, fractional samples give no real indication of an increase in volume of secretion. The introduction of alkalis, as of any substance, probably stimulates gastric secretion, and this is suggested by the rapid dilution of the dye; but, if this is immediately neutralised by alkali

still present, it is not harmful to the patient, and it did not affect the purpose of these experiments, which was to determine whether there was a rebound secretion which might be deleterious after the alkali had left the stomach. Although the volume of secretion could not be measured, such an effect would be shown by a late rise in free HCl concentration.

It is apparent that under the conditions of these experiments there is no evidence of a rebound secretion of acid within two and a half hours after the introduction of the dye into the stomach. Column F in the table shows the higher free HCl concentration in either of the two specimens withdrawn before the introduction of the alkali. In 8 cases the highest concentration of acid found in any of the five fractional samples (columns G–K) was less than this initial reading. In the other 8 it was higher, but in only 2 was it greater by more than 20 m.eq. per litre, and in view of the normal variation in fasting secretion these differences are not significant. In previously published reports it is usually said that only the soluble alkalis cause the rebound secretion; in the present material it is quite clear that sodium bicarbonate does not cause a rebound secretion, for in only 2 of the cases in this group was the highest concentration in the fractional samples greater than before the introduction of the alkalis.

The general pattern of response in individual cases is variable, as can be seen from the table; but on the whole, as long as alkali remains in the stomach, as indicated by the presence of the dye, the stomach contents are alkaline, or only a very low free HCl concentration is found. In most cases all the dye (and alkali) had left the stomach between one and a half and two hours after its introduction, and thereafter no significant increase in free HCl concentration was observed.

The sodium-bicarbonate group of cases includes 3 (nos. 1, 2, and 3) with hypersecretion to the histamine test, and in these the pattern of response is similar to that of the rest. In addition the average response to histamine is considerably higher in this group than in the magnesium-trisilicate group. This is of interest in view of the fact that the response to histamine gives a good indication of the secretory capacity of the stomach to other stimuli (Hunt 1952), and if a rebound secretion did occur it should be most evident in these cases. In this small group of patients with hypersecretion the dye (and alkali) did not leave the stomach any more quickly than in the rest; nor was there any difference in emptying time between the sodium-bicarbonate and magnesium-trisilicate groups, which is in agreement with the findings of Lockwood and Chamberlin (1923).

There are slight differences in the two groups which are of interest. In the sodium-bicarbonate group free HCl was demonstrated in only 1 case while the dye and alkali were still present in the stomach, whereas it was demonstrated, albeit in low concentration, in 6 cases in the magnesium-trisilicate group. Sodium bicarbonate is more efficient as a neutralising agent, for in-vitro studies show that 0·85 g. of sodium bicarbonate is equivalent to 1·2 g. of magnesium trisilicate (Johnson and Duncan 1945). This may explain some of the difference, but some of it may also be due to poor mixing of the insoluble magnesium trisilicate. Sodium bicarbonate is soluble in low concentrations, and it is reasonable to assume that it was present in all the samples in which the dye could be detected. Magnesium trisilicate, on the other hand, is insoluble and consequently it can only neutralise gastric contents with which it comes into contact. In this respect case 9 is of interest, for in the sample withdrawn after half an hour free HCl was present in a concentration of 12 m.eq. per litre yet after an hour the sample was alkaline. In this second sample a lot of magnesium trisilicate was withdrawn; this must have been present in the stomach when the first sample was obtained, and yet because of poor mixing it had not neutralised all the acid that had been secreted.

Discussion

These experiments have shown that there is no evidence to support the theory of a rebound secretion when alkali is introduced into the fasting stomach. After two and a half hours further food will normally be taken, and this will so alter the pattern of gastric secretion that it would be difficult or impossible to determine whether the prior ingestion of alkali had any delayed effect. The only exception to this will be at night, and a preliminary attempt has been made to determine its effect on basal nocturnal secretion. This test was made in 3 patients after 8 g. of sodium bicarbonate had been given two hours before the beginning of the test, and the results were compared with control tests. In these 3 patients the total volume of secretion was essentially the same as in the controls, but in all of them the total amount of free

RESULTS OF FRACTIONAL ANALYSES OF STOMACH CONTENTS

	No.	Age (yr.)	Sex	Diagnosis	Histamine secretion* (ml.)	Resting secretion† (m.eq. per litre)	Fractional samples after introduction of alkali ‡ (m.eq. per litre)					Time when acid was first detected	Time when no more dye was detected	Greatest acid concentration after alkali compared with greatest concentration before alkali
							½ hr.	1 hr.	1½ hr.	2 hr.	2½ hr.			
Col.	A	B	C	D	E	F	G	H	I	J	K	L	M	N
Sodium-bicarbonate group	1	33	F	Duodenal ulcer	320	38	abs (4%)	28 (tr)	48 (tr)	45 (−)	35 (−)	1 hr.	2 hr.	> by 10 m.eq. per litre
	2	35	M	,,	264	41	abs (17%)	abs (4%)	abs (tr)	abs (−)	12 (−)	2½ hr.	2 hr.	<
	3	24	M	,,	210	30	abs (6%)	abs (tr)	abs (−)	16 (−)	19 (−)	2 hr.	1½ hr.	<
	4	34	M	,,	176	16	abs (+)	abs (+)	abs (tr)	abs (−)	abs (−)	..	2 hr.	<
	5	26	M	Psychoneurosis	170	8	abs (6%)	abs (1%)	abs (−)	abs (−)	abs (−)	..	1½ hr.	<
	6	54	M	Duodenal ulcer	155	19	abs (8%)	abs (4%)	4 (−)	4 (−)	15 (−)	1½ hr.	1½ hr.	<
	7	39	M	,,	108	63	abs (1%)	15 (−)	30 (−)	32 (−)	47 (−)	1 hr.	1 hr.	<
	8	34	M	Psychoneurosis	95	4	abs (3%)	abs (tr)	abs (−)	abs (−)	15 (−)	2½ hr.	1½ hr.	> by 11 m.eq. per litre
Magnesium-trisilicate group	9	52	M	Duodenal ulcer	180	59	12 (1%)	abs (tr)	49 (tr)	55 (−)	63 (−)	½ hr.	2 hr.	> by 4 m.eq. per litre
	10	37	M	,,	157	34	abs (10%)	44 (tr)	48 (−)	54 (−)	40 (−)	1 hr.	1½ hr.	> by 20 m.eq. per litre
	11	29	F	Pyloric ulcer	154	34	12 (2%)	19 (tr)	41 (−)	39 (−)	40 (−)	½ hr.	1½ hr.	> by 7 m.eq. per litre
	12	33	M	Duodenal ulcer	139	70	8 (1%)	22 (tr)	17 (−)	54 (−)	69 (−)	½ hr.	1½ hr.	<
	13	24	M	Psychoneurosis	130	29	abs (4%)	12 (tr)	44 (−)	56 (−)	..	1 hr.	1½ hr.	> by 27 m.eq. per litre
	14	27	M	Duodenal ulcer	114	42	abs (45%)	abs (5%)	abs (tr)	39 (−)	50 (−)	2 hr.	2 hr.	> by 8 m.eq. per litre
	15	43	M	,,	109	13	abs (2%)	9 (tr)	4 (tr)	16 (−)	26 (−)	1 hr.	2 hr.	> by 13 m. eq. per litre
	16	57	M	Pyloric ulcer	58	4	abs (6%)	abs (3%)	abs (tr)	abs (tr)	4 (−)	2½ hr.	2½ hr.	<

* Volume of secretion obtained by continuous suction for 1 hour after 0·5 mg. of histamine.
† Greater concentration of free acid in either of the two samples obtained before introduction of alkali.
‡ Concentration of free acid in m.eq. per litre obtained at ½-hour intervals after introduction of 8 g. of alkali. Percentage reduction in concentration of dye is given in parentheses: abs, no free acid present; (tr), trace only—i.e., <1%.

HCl was less. The differences were not significant, but at least they were not greater. The basal nocturnal secretion is notoriously variable when repeated on the same patient, and to get a satisfactory answer an enormous number would have to be examined. In view of these preliminary results and in the absence of any reliable evidence in man to suggest that it may be raised after the ingestion of alkalis the problem has not been pursued.

Earlier work in man is difficult to analyse, because in most instances the alkali was given before or with a test-meal, and usually the results have been recorded on an insufficient number of cases. Crohn (1918) gave sodium bicarbonate and magnesium oxide before a gruel test-meal, comparing the acidity concentrations subsequently reached with those obtained in an earlier control test. He found that the increase in acidity concentrations after the administration of the meal was usually greater and often lasted longer than in the control test. However, he made no allowance for daily individual variability, and in any case the differences that he records would not now be considered significant in view of the fact that reproducible values are not obtained in repeated gruel tests in the same person. In a later experiment Crohn gave magnesium oxide at the end of the test-meal and found that it caused a rapid and efficient neutralisation without any secondary increase in acidity.

Lockwood and Chamberlin (1923) also made fractional analyses on patients to whom alkali had been given with an Ewald test-meal, comparing the results with a previous control test-meal. They found that with sodium bicarbonate the subsequent maximal acidity was greater in half the cases; with calcium carbonate it was greater in a quarter; and with magnesium oxide it was greater in a fifth. These workers are cited in published reports as producing evidence in favour of a rebound secretion; yet their results are no more in favour than they are against—they are very much what one would expect to find by chance.

Keefer and Bloomfield (1926) used alcohol as the gastric stimulus, comparing results with and without the coincidental administration of sodium bicarbonate. They concluded that the sodium bicarbonate caused neither an increase nor a decrease in the volume of gastric juice secreted. They also found that the time taken for free acid to reappear varied with the rate of emptying, which is in agreement with the present results.

Berk et al. (1943) measured the effect of alkalis on the pH in the stomach and duodenum. They passed a double-lumened tube and then, after a short resting period, gave their patients an Ewald test-meal followed later by alkali. They found that there was sometimes a rebound fall in duodenal pH, but from their figures this was not evident in the stomach. They do not attempt to explain this anomaly, but their experiments were rather complicated, and it is difficult to believe that any real rebound secretion would not have been shown in the analyses of stomach contents.

Finally, Breuhaus et al. (1950) compared the effect of various alkalis on the night secretion in 3 normal persons and 6 patients with duodenal ulcers. There was no definite pattern, but by averaging results they found an increase in volume of secretion and a fall in pH in the duodenal ulcer patients after calcium carbonate; this, however, was evident neither in the normal people nor in any instance where insoluble alkalis were given. In an addendum they state that the fall in pH was statistically significant, but they do not mention whether the increase in volume was significant; hence one can only assume that it was not, and in any case they did not have a sufficient number of cases for statistical analysis.

These are the main experimental data in man on which the theory of rebound secretion is upheld. It can be seen that not all the workers support the theory, and those that do have slender reasons. Other evidence in favour of the theory comes from work on dogs with Pavlov or similar pouches. The problem here is entirely different from the work on man; and, so far as has been ascertained, no comparable work has been done on man. Boyd (1925), Alley (1934), and Clark and Adams (1947) have reported experiments on this subject, and although they differ in detail they are essentially similar. They measured the amount of secretion from the pouches, comparing the effect before and after the administration of alkalis. The alkalis were given with or without food and often for several days; in addition the amount given was usually relatively greater than that used in human experiments or in clinical treatment. They found that with the soluble alkalis, but not with the insoluble ones, the volume of secretion from the pouches was significantly greater. Apperly and Crabtree (1931) have shown that gastric secretion is increased when there is a rise in plasma-bicarbonate level. Clark and Adams (1947) found the plasma-bicarbonate level raised in their dogs, and this seems to be a possible explanation of the increased secretion. The dogs, besides being given soluble alkalis, were losing acid from their pouches, and it is hardly surprising that there was such an increase in the alkali reserve. Because of the risk of alkalosis the soluble alkalis are not used often or in large doses in man; and, if this explanation is correct, there should not be any fear of an increase in gastric secretion in patients given insoluble alkalis or soluble ones in reasonable doses.

Summary

Sodium bicarbonate and magnesium trisilicate were introduced into the fasting stomachs of 16 patients, and fractional samples were analysed for two and a half hours.

Free acid reappeared as soon as the alkali had been neutralised or had left the stomach, and it did so in concentrations similar to those present before the alkalis were introduced.

No evidence was found of a rebound secretion of acid within this period.

Earlier work in man and dogs is briefly reviewed. It is suggested that, in the light of modern knowledge on the variability of human gastric secretion, no reliable evidence exists to support the theory of rebound secretion in man when alkali is given in reasonable doses.

In dogs there is an increased gastric secretion when soluble alkalis are given in large doses for a long time, and it is suggested that this is due to an increase in alkali reserve.

So long as soluble alkalis are not given in large doses in man, there should be no fear of any increase in gastric secretion.

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VASODILATATION PRODUCED BY EXPERIMENTAL ARTERIAL GAS EMBOLISM IN MAN

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IN the course of an investigation into the local effects of carbon dioxide on the peripheral blood-vessels in man it was decided, as one method of administration, to inject small quantities of gaseous carbon dioxide into the brachial artery. This was found to produce a large, slowly developing, and very prolonged increase in blood-flow through the forearm. On the other hand, injections of equal quantities of carbon dioxide dissolved in isotonic saline solution were without effect on the blood-flow, and larger quantities produced only a brief increase, the resting level being nearly regained in 2 minutes. This suggested that some of the gaseous carbon dioxide failed to dissolve quickly, and remained as bubbles in the blood-vessels, and that the effects were a consequence of the resulting gas emboli. As this was of considerable theoretical interest, and suggested possible practical applications in therapy, the phenomenon was investigated further. A similar result was obtained on intra-arterial injection of other gases and this paper describes the effects of carbon dioxide, nitrous oxide, cyclopropane, and acetylene on the forearm and hand circulation.

Methods

The subjects were ourselves, our colleagues, and medical students.

The room-temperature was 18°–20°C. A short-bevel needle, 1 mm. in external diameter, was inserted into the brachial artery at the elbow of one side through a small area of anæsthetised skin, and connected by a length of 'Polythene' tubing to a mechanically driven syringe. Sterile physiological saline solution was infused at 2 ml. per minute throughout the experiment. Interposed between the syringe and the polythene tubing was a T-tap through which the gas under investigation could be added to the saline infusion without the subject's knowledge. The gas was introduced manually from a syringe, sealed with saline solution, either as a single injection of 1 or 5 ml. over 15–20 seconds, or as a series of up to 10 injections each of 1 ml. given at intervals of 1 minute. All gas volumes were measured at room temperature and pressure. Because of the compressibility of the gases and the fluctuating arterial pressure a perfectly uniform rate of administration was unattainable.

In most of the experiments blood-flow was measured by venous-occlusion plethysmography. Water-filled and mechanically stirred plethysmographs were applied to the forearms or the hands and kept at 34° or 32°C respectively. The collecting pressure was 70 mm. Hg, and a wrist cuff was inflated to 200 mm. Hg for 1 minute before and during the recording of forearm flows. Recordings were made four times a minute, and each point in the accompanying figures represents the average of the four observations made during the corresponding minute.

In some experiments the circulatory changes in the hands were followed by measuring the rate of heat elimination to a calorimeter at 29°C (Greenfield and Scarborough 1949), and in others the temperature of the skin at various points on the hands was determined with a thermo-electric junction. In all cases the opposite limb was used as a control, so that any variations in the circulation due to vasomotor or blood-pressure changes could be taken into consideration in the interpretation of the results.

The oxygen, nitrous oxide, cyclopropane, and acetylene were supplied by the British Oxygen Company. The first three were of normal anæsthetic grade. The acetylene was commercial-quality dissolved acetylene, the main impurities being about 1% by volume of air and about 3% by volume of acetone vapour. The carbon dioxide was supplied by the Carbon Dioxide Co. Ltd., Liverpool.

Results

OBSERVATIONS ON FOREARM

Fig. 1 shows typical records of the forearm blood-flow measured by venous-occlusion plethysmography before and after the first of 5 injections at minute intervals of 1 ml. of nitrous oxide into the left brachial artery. The resting flows, measured in millilitres per 100 ml. of forearm per minute, were almost the same on the two sides (left 2·9, 2·8, right 3·1, 3·7). The first effect of the injection of the gas was to reduce the flow on the left side to 0·6, that on the right remaining almost unchanged at 2·4. After 24 minutes, however, the flow on the left side had increased to 12·8 and 13·2, while the flow through the right forearm still remained almost unchanged at 2·8 and 3·0.

Fig. 2 represents the response of the forearm flow to 5 injections at minute intervals of 1 ml. of nitrous oxide. The initial reduction in flow was very slight. The subsequent increase in flow reached a maximum in 14 minutes, when the flow was four times that in the opposite forearm. 74 minutes after the injection the flow was still double that in the opposite forearm. A second series of gas injections then caused a second increase in flow to three times that in the control arm. It can be seen that the insertion of the needle, and the infusion of saline solution at 2 ml. per minute, which continued throughout the period of observation, had only a trivial effect on the forearm flow, and that the flow through the control arm was at a steady level throughout.

In the experiment illustrated in fig. 3 the injection of 5·8 ml. of nitrous oxide dissolved in isotonic saline solution was without effect on the forearm blood-flow, but the injection of 5 ml. of the gas produced the usual prolonged increase. For this experiment saline solution was equilibrated by shaking for 10 minutes in an atmosphere of nitrous oxide. At the end of this time analysis in the Van Slyke volumetric apparatus showed 0·58 ml. of dissolved gas per 1 ml. of saline (measured at room temperature and pressure). It is safe to assume that, under these conditions, almost all the dissolved gas was nitrous oxide. Five injections of 2 ml. of this saline

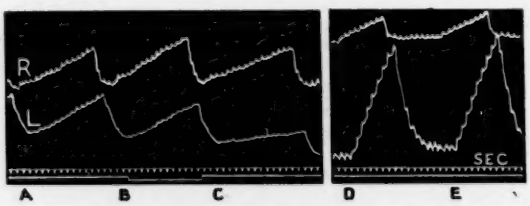

Fig. 1—Typical plethysmograph records of volume changes in the right and left forearms.

Venous-occlusion cuffs, just above elbows, were simultaneously inflated to 70 mm. Hg for 7–12 sec. at A, B, C, D, and E. Rates of volume increase indicate rates of inflow of arterial blood. At A and B rates were about equal on two sides. At the time indicated by the signal the first of five injections at minute intervals of 1 ml. of nitrous oxide was made into left brachial artery. This was followed (C) by decrease in flow on that side. Records at D and E were taken 24 minutes later and show very large flow through injected forearm, flow on control side remaining unchanged.

solution at intervals of 1 minute (a total of 5·8 ml. of nitrous oxide in 10 ml. of saline) were then added to the continuous saline infusion into the brachial artery. This experiment makes it clear that the gas exerts its effect when present as bubbles but is without effect in solution.

Illustrated in fig. 4a is the response to two injections of 5 ml. of carbon dioxide. The second injection, given 10 minutes after the first and when the flow was already increased, produced a second fall in flow followed by a further increase. The flow was still increased 45 minutes after the second injection. In the experiment illustrated in fig. 4b five injections of 1 ml. of carbon dioxide were given at minute intervals. The transient increase which followed the first injection is unusual but has been observed occasionally. When the gas was given in divided doses, as in this experiment, the initial decrease in flow was usually small, but the subsequent increase was similar in size and duration to that produced by a single injection of 5 ml. of the gas.

The effects of the various gases on the forearm blood-flow are shown in fig. 5. In every case there was an increased flow following the injection of the gas whether

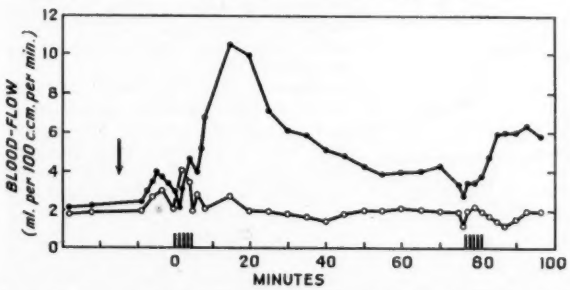

Fig. 2—Forearm blood-flows following intra-arterial injections of nitrous oxide.

Starting at 0 min. and again at 76 min. five injections of 1 ml. of nitrous oxide were given at minute intervals. Arrow indicates time of insertion of arterial needle and start of continuous intra-arterial saline infusion. Solid circles, injected side; open circles, control side.

in single or divided doses, the increase usually being preceded by a fall in flow which varied in degree.

OBSERVATIONS ON HAND

Plethysmographic Observations.—That the injection of gas causes an increase in hand blood-flow is shown in fig. 6. Five injections of 1 ml. of nitrous oxide were given at minute intervals. There was a decrease in blood-flow to below that of the opposite side, followed by a large and prolonged increase.

Calorimetric Observations.—Fig. 7 shows the heat elimination from the whole hand to a calorimeter at 29°C. After five injections of nitrous oxide at intervals of 1 minute there was little or no immediate decrease in the rate of heat elimination, but there was a subsequent increase to more than twice the resting level. The rate of heat elimination then gradually declined, reaching the base-line in about an hour. The rate of heat elimination from the opposite control hand remained at a steady level throughout. These observations confirm the results obtained by plethysmography.

Skin-temperature.—Further confirmation of the increased blood-flow following the intra-arterial injection of gas was obtained by measurement of the skin-temperature at previously selected points on both hands (fig. 8). There was a rise in temperature on the injected side, the extent of the rise being greatest at the peripheral points where the initial temperature was lowest. The temperature on the control side remained unaltered.

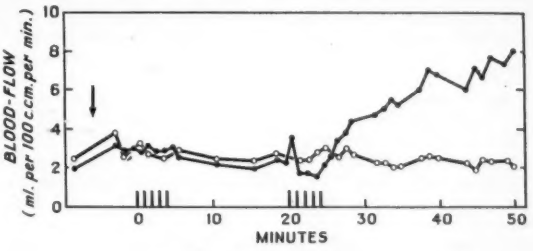

Fig. 3—Forearm blood-flows.

Starting at 0 min. five injections, each of 1 ml. of saline solution containing nitrous oxide in solution (total 5·8 ml. nitrous oxide), were given at minute intervals. At 20 min. five injections, each of 1 ml. of nitrous oxide gas (total 5·0 ml.), were given at minute intervals. Solid circles, injected side; open circles, control side.

COLLECTED RESULTS

The accompanying table summarises the results of all the experiments in which the forearm or hand blood-flow was measured by plethysmography. The injection of the various gases into the brachial artery was always followed by a prolonged increase in blood-flow, but the size and duration of this increase varied with the gas used and from subject to subject.

SKIN COLOUR

In most of the experiments skin-colour changes were observed in the hand while measurements of forearm blood-flow were being made with the plethysmograph. In these experiments the gas was injected into the brachial artery while the circulation to the hand was occluded by inflation of the wrist cuff to 200 mm. Hg. On release of the wrist cuff 5–10 minutes later the control hand showed the normal red flush of reactive hyperæmia, while the experimental hand showed a patchy mottling, with red, white, and blue areas. Evidently some gas had remained trapped in the arteries at the wrist and had passed into the hand on release of the cuff. Within a few minutes further scattered red

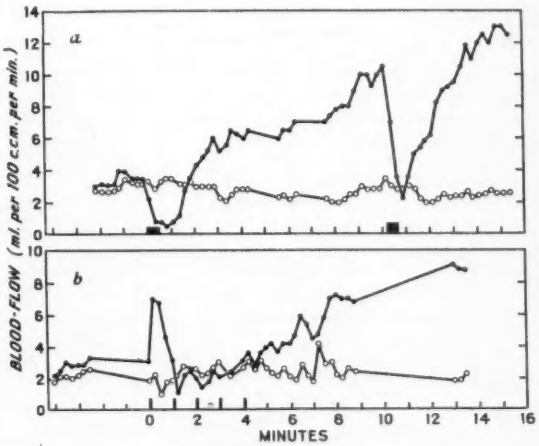

Fig. 4—Forearm blood-flows.

In this figure only, every individual observation of flow is plotted, and not the minute averages: *a*, single injections of 5 ml. of carbon dioxide at 0 min. and 10 min.; *b*, five injections, each of 1 ml. of carbon dioxide, starting at 0 min.; solid circles, injected side; open circles, control side.

patches appeared in the white and blue areas. These gradually became confluent, and within 10–15 minutes (during which the wrist cuff was inflated for 2 minutes in every 5) the whole hand became red. In one case, however, after the injection of cyclopropane, the index and middle fingers and the adjacent part of the hand remained blanched and cold for 25 minutes while the rest of the hand soon became red and warm. Vigorous " milking " of the fingers centripetally led to rapid flushing, presumably by dislodging the gas emboli.

In only one of the 31 experiments did the subject suffer any unpleasant sensation. This subject complained of severe pain in the forearm, which disappeared on removal of the needle, but it is not clear whether it was caused by the needle or the gas. In the other experiments the subject often became aware, after some time, of the warmth of the injected limb, and one subject felt a " crepitation passing into the fingers " shortly after the injection of the gas.

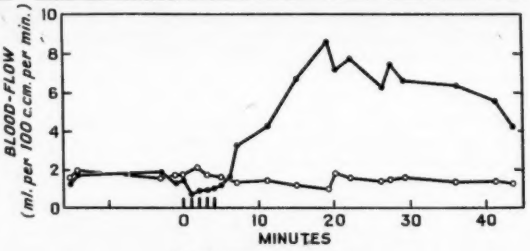

Fig. 6—Hand blood-flows.

Five injections of 1 ml. of nitrous oxide at intervals of 1 minute, starting at 0 min. Needle was inserted and saline infusion started 20 minutes before 0 min. Solid circles, injected hand ; open circles, control hand.

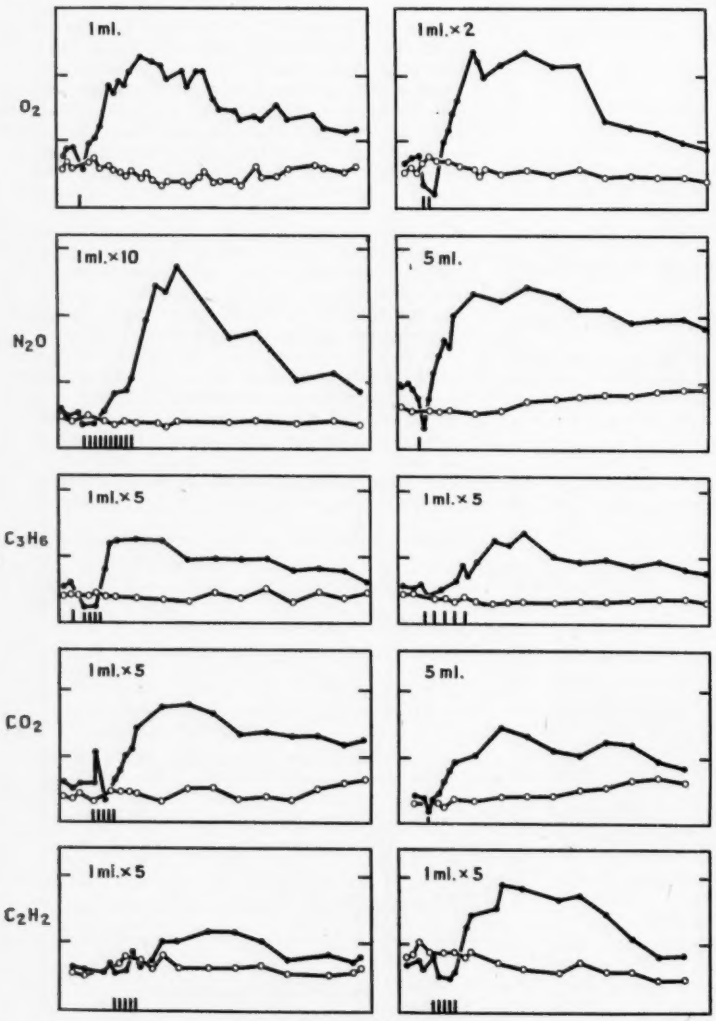

Fig. 5—Forearm blood-flows.

Full height of each frame 15 ml./100 ml./min. ; full width of each frame 1 hour ; solid circles, injected side ; open circles, control side ; doses are indicated in each frame.

Discussion

These observations made by three independent methods show that in normal persons the injection of gas into the brachial artery causes a substantial increase in the blood-flow through the forearm and hand. As the blood-flow remains unchanged in the control limb, the increase must be due to local vasodilatation.

Observations of skin colour indicate that the vasodilatation is patchy, at any rate to begin with. We suggest that the gas forms emboli which block some of the peripheral arteries, arterioles, or capillaries and causes in this way the initial decrease in flow which is commonly seen. Whether these bubbles persist and in some way cause an increase in flow through their still patent neighbours, or whether the increase in flow is through the vessels which were initially blocked, is as yet uncertain. Cyanotic and pale patches in the skin are certainly present when the total blood-flow through the limb is increased.

The gases employed have very different pharmacological properties in solution. Their injection into the brachial artery, however, produces results which are very similar. Moreover, carbon dioxide and nitrous oxide in the doses used in these experiments have a negligible effect when given in solution instead of as gas. These considerations suggest that the effects of intra-arterial injections of gas are produced by the presence of bubbles and are independent of the type of gas in the bubbles or in solution around them.

The rate of disappearance of bubbles of gas in the circulation depends on a complex interrelationship of many variables. Of these the most important are probably the solubility of the gas in blood ; the amount of the gas, if any, already in the blood ; the size of the bubbles ; the rate of passage of blood or tissue fluid past the bubbles ; and the blood-temperature. Less important are the tensions of other gases, already in solution in the blood, which pass into the bubbles until equilibrium is estab-

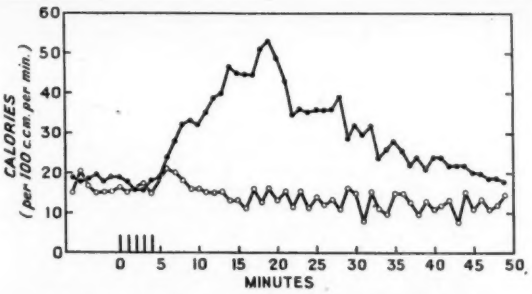

Fig. 7—Heat elimination from whole hand to water at 29° C.

Five injections of 1 ml. of nitrous oxide at intervals of 1 minute, starting at 0 min. Solid circles, injected hand; open circles, control hand.

lished. The gases we have so far used are all freely soluble in blood at body-temperature. The volumes of gas dissolved by one volume of blood at a partial pressure of one atmosphere are as follows:

Acetylene 0·74 (Grollman 1932).
Cyclopropane 0·457 (Orcutt and Seevers 1937).
Nitrous oxide 0·47 (Adriani 1946).

The uptake of carbon dioxide and oxygen by blood depends, of course, mainly on their ability to enter into chemical combination and only slightly on their solubility. We do not yet know whether more persistent vasodilatation could be obtained by the use of less soluble gases such as hydrogen, helium, argon, and nitrogen. Investigation of the effects of these gases in man must obviously proceed with caution.

The way in which the bubbles produce their vasodilator effect is not yet clear. They may release a chemical mediator or operate through a nervous pathway. These possibilities are now being examined experimentally, and the findings will be published elsewhere.

It might be suggested that the increase in flow is similar to the reactive hyperæmia which follows temporary arrest of the circulation. In reactive hyperæmia the blood-flow debt may or may not be completely paid off (Dornhorst and Whelan 1953); but, so far as we know, substantial overpayment of the debt has never been demonstrated. The blood-flow debt incurred during the initial period of decreased flow in these experiments is paid off many times over during the subsequent period of increased flow, and in many cases little or no debt is incurred; so the results of the injection of gas cannot be explained in terms of previous observations on the behaviour of the circulation after periods of arrest.

RESULTS OF PLETHYSMOGRAPHY

Subject		Gas	Dose	Maximum flow (ml. per 100 ml. of tissue per min.)	Control flow (ml. per 100 ml. of tissue per min.)	Time to maximum (min.)
Forearms:						
A.D.M.G.	Feb. 26	O_2	1 ml.	11·2	2·4	12
P.J.T.	March 10	O_2	1 ml. ×3	10·5	2·5	19
A.E.I.	,, 12	O_2	1 ml. ×2	11·5	2·8	11
D.S.McL.	April 24	N_2O	1 ml. +5 ml.	5·8	2·9	13
F.D.	March 6	N_2O	1 ml. +5 ml.	7·1	2·6	20
J.D.A.R.	,, 6	N_2O	5 ml.	11·7	2·7	11
E.B.	,, 31	N_2O	1 ml. ×10	13·7	2·0	19
R.F.W.	May 27	N_2O	1 ml. ×5	10·7	2·5	14
F.D.	,, 28	N_2O	1 ml. ×5	8·0	2·1	29
P.J.G.	April 2	C_2H_4	1 ml. ×5	6·4	2·7	13
W.D.H.	,, 9	C_2H_6	1 ml. ×5	6·6	1·9	21
R.F.W.	Feb. 20	CO_2	1 ml. +5 ml.	11·5	2·8	12
J.M.	,, 25	CO_2	5 ml.	5·6	2·4	12
D.J.L.C.	March 4	CO_2	5 ml.	7·1	2·1	14
P.H.	,, 5	CO_2	5 ml. +5 ml.	13·9	2·5	25
D.J.L.C.	,, 4	CO_2	1 ml.	3·1	1·8	13
J.B.	,, 7	CO_2	1 ml. ×5	9·0	1·8	13
R.F.W.	April 24	C_2H_2	1 ml. ×5	5·9	3·1	20
W.J.W.	,, 29	C_2H_2	1 ml. ×5	9·2	3·7	19
Hands:						
W.D.P.	Feb. 28	O_2	1 ml.	15·2	6·9	17
A.R.B.	April 16	N_2O	1 ml. ×5	8·5	1·0	21
W.D.H.	,, 15	N_2O	1 ml. ×5	4·7	1·0	13
M.O.J.	March 9	CO_2	1 ml. ×5	6·1	2·6	16

Maximum flow is the highest minute average observed following the injection of gas.
Control flow is the simultaneously observed flow in the opposite limb.
Time to maximum is measured from the first injection of gas.

We do not yet know whether the phenomenon is confined to the circulation in the upper limbs or whether it can also be demonstrated in organs such as the heart, brain, and kidneys. In those parts in which it is present the phenomenon may play a very important rôle as a protective mechanism against the obstructive effects of emboli.

Many workers have studied the local and general effects of arterial gas embolism (Durant et al. 1949), but we are unaware of any earlier observations of the prolonged vasodilatation described here.

The dilatation following the injection of gas lasts much longer than that following the injection of such substances as histamine, acetylcholine (Duff, Greenfield, et al. 1953), and magnesium adenosine triphosphate (Duff, Patterson, and Shepherd 1953), and this suggests a possible therapeutic application. We have not yet defined the best dose or the best gas for a maximal response. It must be borne in mind that, although the total flow of blood through the whole limb is increased, the flow through certain portions of tissue

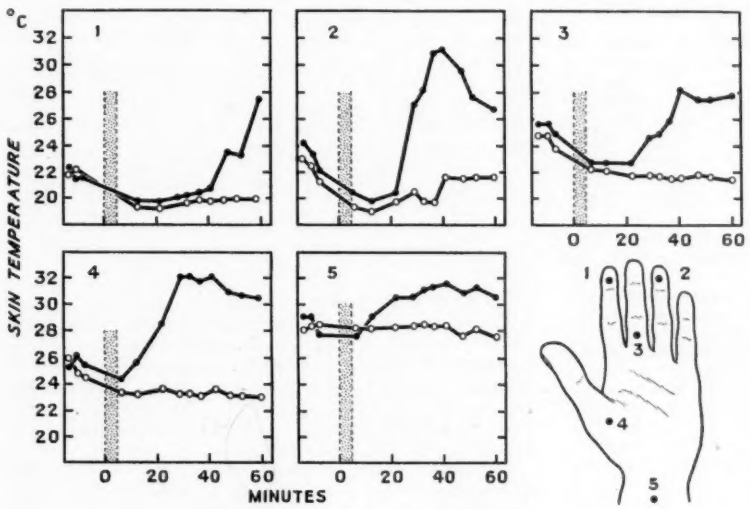

Fig. 8—Skin-temperature at five points on hands.

Five injections of 1 ml. nitrous oxide at intervals of 1 minute during time indicated by shaded column. Solid circles, injected hand; open circles, control hand.

may be greatly diminished. Further investigations and a clinical trial will be necessary to determine these points.

Summary

The injection of a few millilitres of various gases into the brachial artery causes vasodilatation, the blood-flow in the forearm and hand increasing to three to five times the resting level and remaining raised for an hour or more.

This response is the consequence of the presence of gas emboli.

Theoretical and practical implications of the response are briefly discussed.

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Preliminary Communication

PHYSIOLOGICAL ACTIVITY OF THE ACETIC-ACID ANALOGUES OF SOME IODINATED THYRONINES

THE synthesis of the acetic-acid analogue of thyroxine was described by Harington and Pitt-Rivers in 1952[1]; the acetic-acid analogue of triiodothyronine has now been prepared. In this paper the activity of these two compounds and that of the acetic-acid analogue of 3 : 5-diiodothyronine in preventing thiouracil-induced goitre in rats is described; the activity of the triiodo-acid in raising the metabolic-rate of rats is also demonstrated.

For the sake of convenience the three compounds

3 : 5-diiodo-4-(4′-hydroxyphenoxy)phenylacetic acid,
3 : 5-diiodo-4-(3′-iodo-4′-hydroxyphenoxy)phenylacetic acid, and
3 : 5-diiodo-4-(3′ : 5′-diiodo-4′-hydroxyphenoxy)phenylacetic acid

have been named diiodothyroacetic acid, triiodothyroacetic acid, and tetraiodothyroacetic acid respectively.

EXPERIMENTAL METHODS

Synthesis of Triiodothyroacetic Acid

3 : 5-Diiodo-4-(4′-hydroxyphenoxy) phenylacetic acid[1] was iodinated by the method described for the preparation of triiodothyronine by Gross and Pitt-Rivers.[2] The product, which was obtained in 84% yield, was twice crystallised by dissolving in cold methanol and adding an equal volume of cold water; it had an indeterminate melting-point in the neighbourhood of 100°C, but was shown chromatographically to be free from starting material and from the tetraiodo acid. (Found: I, 60·9%; $C_{14}H_9O_4I_3$ requires I, 61·2%.)

Biological Experiments

Goitre prevention assay.—These assays (experiments 1, 2, and 4) were carried out in the way described by Gross and Pitt-Rivers.[3]

Male hooded rats weighing 80 ± 5 g. were divided into groups containing 6 rats, with 2 rats in each cage. All the animals had 0·1% thiouracil and 3% sugar in their drinking-water and were injected subcutaneously with the control solution (saline) or the test solution each day, for nine days. On the tenth day the animals were killed, the thyroid glands were removed and weighed, and the weight of gland per 100 g. body-weight was calculated.

In all three experiments group A was the control group and received injections of saline solution, and group B received injections of 0·4 μg. L-triiodothyronine.

Experiment 1.—Tetraiodothyroacetic acid: groups C, D, and E received 1 μg., 3 μg., and 6 μg. respectively.

1. Harington, C. R., Pitt-Rivers, R. *Biochem. J.* 1952, **50**, 438.
2. Gross, J., Pitt-Rivers, R. *Ibid*, 1953, **53**, 645.
3. Gross, J., Pitt-Rivers, R. *Lancet*, 1952, **i**, 593.

TABLE I—RESULTS OF EXPERIMENT 1

Animal no.	A		B		C		D		E	
	Body-weight (g.)	Thyroid weight (mg.)	Body-weight (g.)	Thyroid weight (mg.)	Body-weight (g.)	Thyroid weight (mg.)	Body-weight (g.)	Thyroid weight (mg.)	Body-weight (g.)	Thyroid weight (mg.)
1	122	33·0	119	12·3	122	19·5	123	16·0	111	11·6
2	117	31·2	121	12·5	115	21·9	120	14·3	114	9·6
3	125	31·2	124	9·7	126	31·4	124	19·5	143	10·3
4	124	31·1	112	14·2	132	22·9	122	15·6	114	12·0
5	122	26·8	110	11·8	115	18·9	132	13·8	98	8·4
6	118	27·3	130	21·6	118	20·4	108	14·5	127	12·8

Experiment 2.—Triiodothyroacetic acid: groups W, X, Y, and Z received 0·5 μg., 1 μg., 3 μg., and 6 μg. respectively.

Experiment 4.—Diiodothyroacetic acid: groups C, D, E, and F received 0·5 μg., 1 μg., 4 μg., and 20 μg. respectively.

Effect of triiodothyroacetic acid on oxygen consumption in intact rats.—Four groups of 6 male hooded rats weighing 40–44 g. were kept in a room at 29° ± 1°C for three days to acclimatise them to the temperature and were then given one day of training in the metabolism apparatus which was kept in the same room (experiment 3). The apparatus was that used by Tomich and Woollett[4] and the method is a modification of the technique of Maclagan and Sheahan.[5] All measurements were made on individual rats. The basal O_2 consumptions of rats in all the groups were determined on four consecutive days, and on the fifth day injections were started. (At this point 1 rat had to be discarded from group B owing to continued extreme nervousness when placed in the metabolism chamber.) Groups A and C received 50 μg. and 20 μg. L-triiodothyronine respectively; groups B and D received 250 μg. and 100 μg. triiodothyroacetic acid respectively. All injections were given daily.

Determinations of oxygen consumption were resumed forty-eight hours after the first injections. In group A treatment was discontinued after three daily injections because of the condition of the animals, which all appeared sick; for the same reason group-B rats were treated for only four consecutive days. Groups C and D rats received treatment for five days, except for 1 rat in group C which became so ill that it had to be removed from the test.

TABLE II—RESULTS OF EXPERIMENT 2

Animal no.	A		B		W		X		Y		Z	
	Body-weight (g.)	Thyroid weight (mg.)	Body-weight (g.)	Thyroid weight (mg.)	Body-weight (g.)	Thyroid weight (mg.)	Body-weight (g.)	Thyroid weight (mg.)	Body-weight (g.)	Thyroid weight (mg.)	Body-weight (g.)	Thyroid weight (mg.)
1	117	32·5	110	8·8	100	26·4	125	24·9	110	16·8	128	16·7
2	120	33·0	98	10·2	110	26·2	116	21·4	109	19·0	129	9·4
3	132	32·8	129	21·1	119	20·0	118	28·0	119	22·6	115	12·6
4	109	32·4	101	10·2	125	23·9	110	23·5	136	20·5	99	9·8
5	124	38·1	128	13·6	116	28·1	126	23·4	110	18·8	107	10·9
6	131	30·2	120	18·0	120	24·3	103	21·5	120	9·0	127	10·2

RESULTS

Goitre Prevention Assays

The effects of tetraiodothyroacetic acid and triiodothyroacetic acid are shown in tables I and II, and the potencies of the two compounds compared with that of L-triiodothyronine have been calculated. The value for the tetraiodo acid is 0·104 and for the triiodo acid 0·087 (L-triiodothyronine = 1); there is no significant difference between the two results.

Diiodothyroacetic acid was quite inactive even at the highest dose level; its activity is therefore less than one-fiftieth of that of triiodothyronine; from the weights of the thyroids of rats in group F of experiment 4 its

4. Tomich, E. G., Woollett, E. A. *Ibid*, 1953, **i**, 726.
5. Maclagan, N. F., Sheahan, M. M. *J. Endocrin.* 1950, **6**, 456.

activity is probably very much lower, since there was no difference between the weights of these thyroids and those in the control (A) group.

Effect of Triiodothyroacetic Acid on Oxygen Consumption

The results are shown in table III. Because of the high mortality in groups A and B (high dose levels of triiodothyronine and triiodothyroacetic acid) it has not been possible to calculate the relative potencies of the two compounds; nevertheless it appears from the results that the acetic-acid derivative has considerable activity in increasing the metabolic-rate in rats.

DISCUSSION

The high degree of activity of the acetic-acid analogues of thyroxine and triiodothyronine in the goitre-prevention assay and of the latter in raising the metabolic-rate of rats might at first seem surprising; the only other thyroxine analogue with a 2-carbon atom side-chain to be tested, the glycine analogue, has been shown by Frieden and Winzler [6] to be almost devoid of thyroidal activity in mammals. Nevertheless the normal metabolic process whereby amino-acids are converted by amino-acid oxidases to the corresponding acetic acids might well be involved in the metabolism of thyroxine and triiodothyronine, although no enzyme system has yet been found which can achieve this process in vitro. Tetraiodothyroacetic acid and triiodothyroacetic acid are not yet known to occur as natural compounds, and no evidence at present exists to support the hypothesis that these are a part of the series of reactions involved in the biosynthesis of the thyroid hormone, except for their suggestively high biological activity. Experiments are at present being undertaken to determine whether either or both of these acetic acids can replace thyroxine and triiodothyronine in the thyroidectomised animal; if they can, it will be strong presumptive evidence that they have a place in the biosynthetic or metabolic chemistry of the thyroid hormone.

TABLE III—RESULTS OF EXPERIMENT 3

Percentage rise in O_2 consumption measured at different times after the first injection (number of animals in parentheses)

Group	O_2 consumption before treatment (ml. O_2 per g. body-weight per hr.)*	Hours after first injection									
		48	54	72	78	96	102	120	126	144	150
A	1·62 (6)	58(6)		71(5)		77(1)		70(1)		27(1)	
B	1·55 (5)	74(5)		75(5)		69(2)		57(2)		29(2)	
C	1·64 (6)		49(6)		55(5)		56(5)				55(5
D	1·61 (6)		43(6)		58(6)		51(6)				27(6)

* The values for basal oxygen consumption are the average of four days' values.

SUMMARY

The acetic-acid analogues of thyroxine, triiodothyronine, and diiodothyronine have been assayed by the goitre-prevention method. Tetraiodothyroacetic acid and triiodothyroacetic acid both possess about one-tenth of the activity of L-triiodothyronine. Diiodothyroacetic acid is relatively inactive in this assay.

Triiodothyroacetic acid has been shown to have considerable activity in increasing the metabolic-rate of rats.

I wish to thank Miss S. McBride and Mr. A. D. Brownstone for help with the biological experiments, and Miss M. V. Mussett for the calculations of the results. I also wish to thank Mr. E. G. Tomich, of Glaxo Laboratories Ltd., for the loan of his metabolism apparatus and for instruction in its use.

National Institute for Medical Research, Mill Hill, London — ROSALIND PITT-RIVERS M.Sc., Ph.D. Lond.

6. Frieden, E., Winzler, R. J. *J. biol. Chem.* 1948, **176**, 155.

Reviews of Books

The Work of Sir Robert McCarrison

Editor: H. M. SINCLAIR. London: Faber & Faber. 1953. Pp. 327. 30*s*.

THE young investigator today finds it difficult enough to keep abreast with the writings of his contemporaries and almost impossible to read systematically the works of the great men of the previous generation. These often appeared in journals that are now obscure or in books that are out of print, and the fundamental work is sometimes much diluted by what time has proved to be unimportant, which makes the task doubly difficult. Dr. Sinclair has done very well to condense Sir Robert McCarrison's 9 books and 159 papers into 320 pages. McCarrison's contributions to our knowledge of the thyroid gland and the deficiency diseases give him a secure place in the history of medicine: and his writings, now available in this convenient form, well deserve study today.

The mass of epidemiological material in India, and the first-class conditions for keeping large numbers of experimental animals at Coonoor, provided McCarrison with the opportunity. He set out to reproduce in these animals both the dietary and the hygienic conditions of the peoples of India. He trained himself as a morbid histologist and was able to demonstrate the manifold effects of a faulty diet and adverse environment on the tissues of the body. Avoiding the oversimplications so often made in the more elaborately equipped European and American laboratories, he has always emphasised that a lack of iodine and vitamins, though of fundamental importance in the production of goitres and deficiency diseases, is seldom the whole story. In an essentially modern way, he repeatedly demonstrated in the field and in the laboratory that a variety of stresses and strains determine the body's requirements of these essentials. In practice, diseases often result from a subtle disturbance of a balance between an uncertain supply and extraordinary demands. Further, McCarrison was ever aware of the possibilities of preventive medicine and so designed his experiments that they might give results of practical value to the people of India.

Happily this book was available for Sir Robert's 75th birthday, and W. R. Aykroyd, E. V. McCollum, and the editor offer elegant tributes.

Principles of Thoracic Anæsthesia: Past and Present

WILLIAM W. MUSHIN, M.A. Oxfd, M.B. Lond., F.F.A. R.C.S., director of anæsthetics, Welsh National School of Medicine; L. RENDELL-BAKER, M.B. Lond., D.A., consultant anæsthetist, United Cardiff Hospitals. Oxford: Blackwell Scientific Publications. 1953. Pp. 172. 42*s*.

THIS history of thoracic anæsthesia will interest all doctors who deal with diseases of the chest, anæsthetists and surgeons in particular. The techniques of anæsthesia used for thoracic work are also commonly used, nowadays, for operations on other parts of the body.

The apparent simplicity of many modern methods based on aided or controlled respiration is apt to mislead onlookers into rating too lightly the responsibilities of the anæsthetist. Simple these techniques may be, but their proper use and the consequent safety of the patient depend on a wide knowledge of the basic sciences, and a considerable practical experience in the operating-theatre. It is a striking fact, brought out fully in this book, that the problem of the open thorax delayed the progress of thoracic surgery for many years, and the solution eluded the brains of men of the calibre of Matas and Sauerbruch for over fifty.

The theme of the work is the pneumothorax problem. The story is developed from the earliest attempts at resuscitation of the drowned by manual inflation of the lungs, through the stage of positive pressure and insufflation anæsthesia, to the modern technique of rhythmic inflation either by hand or by an automatic device. The chapter on tracheal and bronchial intubation, and on the control of secretions, is largely a chronological list of the various developments in these fields. Almost the whole work is concerned with the historical evolution of this branch of anæsthesia: details of present-

day methods, and the arguments for and against individual agents, are not given, but the various modern mechanical devices are described sufficiently to make their mechanisms easily understood.

This work, as the authors specifically state in their preface, is not intended to be a "how-to-do-it" book. It is, in fact, a contribution to the literature of medicine, simply written and particularly well illustrated.

Clinical Psychiatry for Practitioners and Students

IAN SKOTTOWE, M.D. Glasg., M.R.C.P., D.P.M., psychiatrist, Warneford and Park Hospitals, Oxford. London: Published for the *Practitioner* by Eyre & Spottiswoode. 1953. Pp. 395. 36*s*.

Dr. Skottowe has added one more to the textbooks on psychiatry. To justify such a deed, an author should be fresh and up to date as well as being accurate; and these tests Dr. Skottowe and his book pass with distinction. He demonstrates well the intimate links between psychiatry and general medical problems, giving examples —though not nearly enough—of ways in which numerous physical examinations can increase rather than diminish a patient's anxiety. He reminds us how often "pain" is a complaint of the patient who is trying to express a disorder of general well-being, and how a history-taking of all symptoms may help the doctor to hear nuances of those physical symptoms which are psychically determined. His account of children's psychological disorders might have been longer with advantage. His title prompts us to ask whether psychiatry can, in fact, be written "for practitioners and students" jointly. Many good attempts have been made, and this is one of them; but none has been fully satisfactory. Is it possible to envisage a textbook in two parts, the first the straightforward basis for the student—as simple as it can be—while the second discusses for qualified men vaguer yet no less essential problems such as the approach to the psychiatric patient's relatives, the difficulties presented by his environment, how much the doctor should or can do, and the ways in which symptoms of emotional origin yet physical form can be detected early? Dr. Skottowe's outlook, as revealed in this book, suggests that he could succeed in such a task.

Les groupes sanguins chez l'homme

JACQUES RUFFIÉ, assistant de médecine legale et de médecine du travail, à la Faculté de Médecine de Toulouse. Paris: Masson. 1953. Pp. 207.

THIS is a perfectly straightforward and very up-to-date account of the present knowledge of the blood-groups, including all the various types now known. It is interesting to see that the author prefers the Fisher to the Wiener notation for the Rh subgroups, though he thinks the differences are largely artificial. So much work on this subject has been done in English-speaking countries that oddities like "le crossing-over" and "le facteur anti-Jobbins" are inevitable. As in all books on this subject, statistics soon appear and there are plenty of square-root signs.

Classification of Pulmonary Tuberculosis

MILOSH SEKULICH, M.D. London: Heinemann Medical Books. 1953. Pp. 322. 63*s*.

Dr. Sekulich describes a classification of pulmonary tuberculosis for international use. Unlike others, his method of charting the disease covers the type and extent of the lesion and its degree of activity. Thus a case is noted as being of one of four pathological forms—either inflammatory or caseous (the primary pathogenetic type of tuberculosis), or fibrocaseous or fibrous (the post-primary type). Each of these forms is subdivided into groups. The radiological zones, as laid down in the British classification, define the extent of the lesion. The disease is either active or inactive, evolving or involuting. The presence of tubercle bacilli is also charted. Thus a tuberculoma of primary origin would be represented as: type, primary; form, inflammatory; subform, obsolete form; subgroup, tuberculoma; extent, left mid-zone; activity, quiescent; tubercle bacilli never demonstrated. Which is represented by the formula: I.3.c. LMZ. Quies. A.

This classification employs 29 forms, 6 zones, and 8 degrees of activity. It is a full notation of the disease at a definite period in its course—an abbreviated case-sheet. The principle is methodologically pleasing, and the terminology of disease, extent, and activity conform to conventional standards. Nevertheless universal acceptance of the author's definition of forms of disease may not come easily; for pathological considerations are important in the grouping, and the pathology of tuberculosis is expressed differently in different parts of the world.

A less expensive and perhaps more useful edition of this book could be produced by omitting many of the radiographs and by cutting the text. As published, it is not a monograph on a proposed classification, but a textbook of tuberculosis including the proposals.

Hypnosis in Modern Medicine

Editor: JEROME M. SCHNECK, M.D., clinical associate in psychiatry, College of Medicine, State University of New York. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1953. Pp. 323. 54*s*.

THE choice of hypnosis as a method of treatment is apt at present to depend not so much on the patient's disability or personality type as on the fact that his doctor happens to be interested in the subject.

Scattered throughout the field of medicine and psychiatry there are a number of conditions which can perhaps be dealt with by an experienced hypnotist as well as in any other way. In dentistry, in obstetrics, in the treatment of recent functional disabilities, in some cases of stammering and nocturnal enuresis, and in the restoration of function after immobilisation in plaster, hypnotism is sometimes very successful; but the physician often hesitates to use it either because he has no confidence in his own technique or because of his fear that a specialist in medical hypnosis may be too flamboyant in his approach, or may fail to confine himself to the prescribed objective.

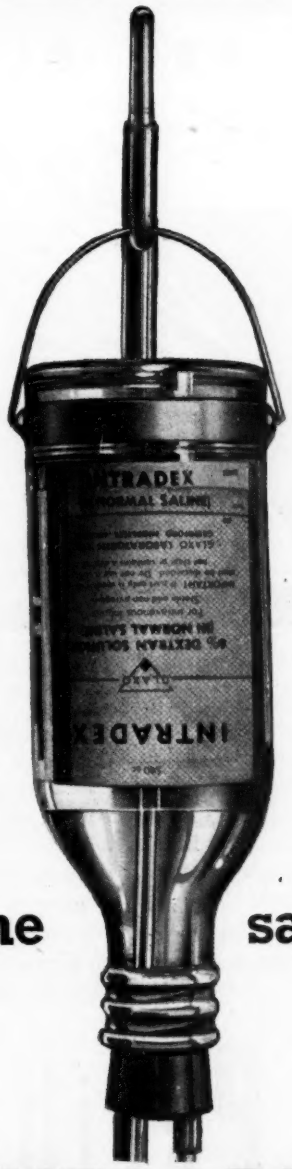
Dr. Schneck's aim is to present to the general medical reader a survey of the contribution that hypnosis can make to his problems and of its indications. There is in addition a general and a historical introduction and a chapter on methods of learning to hypnotise. The writers of the different sections are mainly medical workers who have used hypnosis in their particular field. The quality is varied, and there is far too much duplication and little to allay the impression that the medical hypnotist is apt to claim too much for his method and may sometimes be rather out of touch with current thought in medical and psychiatric matters.

If the number of new books is any guide, hypnosis is having one of the periodic revivals within the profession which have occurred so frequently during the last hundred and fifty years. It is doubtful however whether this volume will preach successfully to any but the converted.

Progress in Neurology and Psychiatry (London: Allen & Unwin. 1953. Pp. 604. 70*s*.).—Volume VII of this annual review, which is edited by Prof. E. A. Spiegel (see *Lancet*, 1952, ii, 1256), has now been published in this country.

Pathology of Tumours (2nd ed. London: Butterworth. 1953. Pp. 997. 84*s*.).—This important book by Prof. R. A. Willis first appeared in 1948 and rapidly and deservedly became a standard work of reference. A new and up-to-date edition will therefore be generally welcomed. Special attention has been paid to the recent work on tumours of chemoreceptors, melanomas, and carcinoma of the bronchus, while the ably written review on cancer research, embodying our knowledge on the carcinogenic hydrocarbons, has been brought up to date.

There are three principal reasons why this work is so popular: Professor Willis makes full use of case-records, reflecting his widespread experience in Melbourne, London, and now in Leeds; his outspoken and able criticism in controversial matters in oncology is directed towards the commendable aim of simplifying existing nomenclature; and he has been at great pains to select the extensive bibliography (400 new references have been added in the present edition). The classification of tumours, a simple and helpful one especially for students, is based on histogenesis and behaviour.



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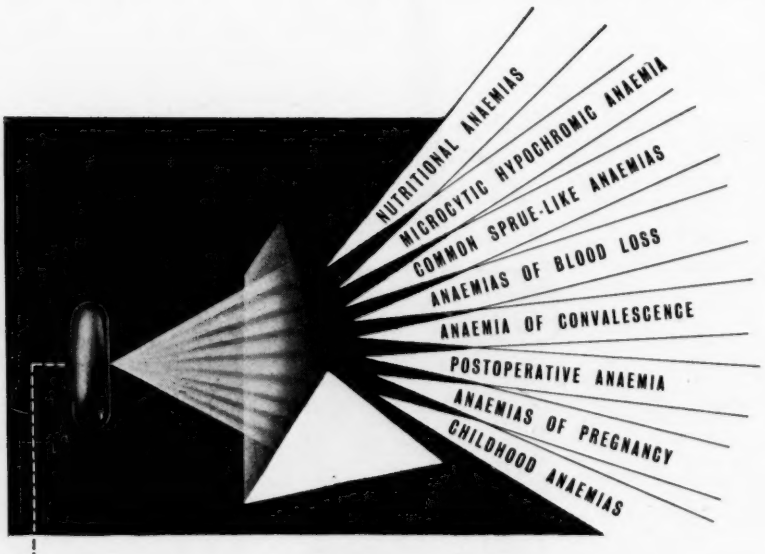

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THE LANCET
LONDON: SATURDAY, AUGUST 1, 1953

The Wrong Blood

Dr. JAMES's review of legal responsibility in blood-transfusion, which we publish on p. 243, is timely because the last few months have seen a disquieting number of reports of incompatible transfusions. Most of these seem to be caused by what even a sympathetic observer would term carelessness. Dr. X or Nurse Y fails to check the label on the bottle because he or she assumes that whoever brought the bottle has seen that it contained the correct blood. A nurse is sent to the laboratory to obtain a bottle of cross-matched blood, but does not know the name of the patient for whom it is wanted; when, in dumb show, the doctor points to a refrigerator, she takes blood selected for a different patient. A nurse takes an unlabelled specimen to the laboratory for grouping and cross-matching, and it is later found that the specimen came from the wrong patient. A nurse, without consulting the blood-bank staff, takes a bottle of blood carrying the patient's name; it turns out that this was the donor's name, not that of the intended recipient. Someone keep blood overnight in the bone-bank refrigerator at −8°C, or in a refrigerator adjusted to store ice-cream. All these accidents have happened at one time or another; and some have been fatal. Such mishaps are the outcome of bad training and bad organisation. Fifteen years ago blood-transfusion was uncommon and therefore the greatest care was taken over it. Mistakes were made, but the deaths were mostly the result of incompatibility that could not be recognised before transfusion. Now that transfusion is commoner, the majority of errors seem to arise from confusion between patients' names, or carelessness in failing to check that the bottle of blood administered is the bottle of blood intended for that particular patient. Only the fatal incompatible transfusions are reported, and perhaps three to fifteen times as many incompatible transfusions are given without leading to the patient's death.[1 2]

This problem closely affects clinical and nursing staffs. Mistakes are made by doctors who have been inadequately taught, or have not been taught, the essentials of blood-grouping and hæmodynamics as applied to transfusion, and Dr. JAMES gives several examples of such lack of knowledge. There is every reason to support his suggestion that "a place in the medical school curriculum should be made for this study, if necessary at the expense of less potentially lethal subjects." Attention will have to be given also to defining nurses' responsibility in blood-transfusion; at present in many hospitals nurses are allowed to change bottles of blood, and in some to change the needles. Junior medical staff are often in a hurry and do not always check the label indicating the patient for whom the bottle is intended. It would seem wise to adopt universally the rule that, before transfusion, each bottle of blood should be checked either by two nurses or by a nurse and a doctor. Proper identification can be assured only if blood samples are clearly labelled. The National Blood Transfusion Service supplies a tie-on label for blood which has been cross-matched for a particular patient; but this carries so much printing that it is not easily completed, while some of the information requested appears to be unnecessary. Furthermore, this label readily gets sodden and then tears or becomes illegible. There is room for ingenious improvement in labelling blood bottles.

There are other possible mistakes. From a recent inquest it appears that a technician responsible for blood-grouping had made an error in rhesus typing. This error might be made by anyone; but he was reported as being unaware that some rhesus antibodies agglutinate cells only in protein-rich media, and that repeated tests in saline solution may reveal no incompatibility even though the patient reacted adversely to the transfusion. There are few consultants in hæmatology, and sometimes the pathologist officially responsible for the hospital blood-bank[3] fails to familiarise himself with the theory or practical techniques of modern blood-grouping: instead he deputes responsibility to a senior hospital medical officer, a registrar, or even a technician. In some hospitals a technician who has spent a fortnight or a month in a regional depot learning techniques is expected to undertake all the blood-grouping work with little or no supervision. This is wrong. Technicians and registrars must not be given such responsibility, because their knowledge is usually insufficient. The pathologist in charge of the blood-bank must be as familiar with modern blood-grouping techniques as are any of his assistants, and to attain the necessary standard may require a third of his working hours for six months; in a large hospital he may need to continue this close attention indefinitely. If a consultant in charge of a blood-bank fails to familiarise himself with the latest ideas, or fails to supervise his assistants and technicians, then, in the event of a transfusion error, he might be found negligent.

Hæmatology and blood-transfusion are usually assigned to the most junior consultant or to a registrar, and regarded as a nuisance. In fact, the man in charge of transfusion can do more damage by carelessness, ignorance, or neglect than can any of his colleagues except perhaps an incompetent surgeon. Transfusion must be under the direct control of a senior pathologist who is prepared to spend much of his time on the unpopular task of organisation, and probably to wage an unpopular war to secure proper provision of buildings, technicians, and, in any busy hospital, resident medical staff.

Resistant Tubercle Bacilli

IN drawing attention once more to the regrettable tendency of bacteria to become resistant to our remedies, the Medical Research Council[4] has lately said that the most encouraging results of attempts to prevent these resistant states have been those obtained in the antibacterial treatment of tuberculosis. Full information about these results will be found in the latest reports of the council's Tuberculosis Research Unit, published earlier in this issue.

Previous reports[5 6] described the first three months' use of various combinations of streptomycin, *p*-amino-

1. Dahr, P. *Langenbecks Arch. klin. Chir.* 1950–51, **266**, 82.
2. Discombe, G. *Lancet*, 1952, i, 734.
3. See Circular R.H.B. (51) 89.
4. Medical Research Council: annual report for 1951–52. H.M. Stationery Office. 1953.
5. Medical Research Council. *Brit. med. J.* 1952, ii, 735.
6. Medical Research Council. *Ibid*, 1953, i, 521.

salicylic acid (P.A.S.), and isoniazid, and we are now given the bacteriological findings after six months. At the end of that period 62% of patients treated with isoniazid alone still had tubercle bacilli in their sputum and in 93% of these the bacilli had become resistant. But of those treated with streptomycin plus isoniazid only 7% (4 of 54) still had a "positive" sputum; 2 of the 4 cultures were sensitive to isoniazid and all to streptomycin. The group receiving streptomycin plus P.A.S. had 18% (8 of 44) positive and 2 of the 7 cultures examined were resistant to streptomycin. Thus isoniazid was quite as effective as P.A.S. in preventing the emergence of streptomycin-resistant strains during six months' treatment. The patients received isoniazid in doses of 200 mg. daily, P.A.S. in doses of 20 g. of the sodium salt daily, and streptomycin by injections of 1 gramme—daily for the first three months but in most cases only three times a week during the second three months. As the emergence of resistance is probably influenced chiefly by the dosage during the early months of treatment any conclusions to be drawn from this English series apply only to a combination of daily doses of the drugs. In the United States Public Health Service trial [7] streptomycin 1 g. was given twice weekly, with either 150–300 mg. isoniazid or 10–12 g. P.A.S. daily, and the results do not seem to have been quite so good. After twenty-four weeks 4 of 27 patients receiving streptomycin plus isoniazid still had a positive sputum, 3 of the cultures being resistant to streptomycin and 2 to isoniazid. Of 28 patients treated with streptomycin plus P.A.S. 10 still had a positive sputum and 7 of the cultures were resistant to streptomycin. But comparison between the bacteriological effects of daily and of intermittent streptomycin, given with isoniazid, cannot yet be made. The emergence of resistant bacilli depends not only on the dosage of the drugs but also on the character of the pulmonary lesions, and two series of patients must be comparable in this respect before differences in bacteriological findings can be attributed to differences in dosage. It would therefore be prudent to wait for the results of the Medical Research Council investigation of the intermittent regimen before adopting it more generally.

Though opinions differ at some points in the antibacterial treatment of tuberculosis, there is no doubt whatever about the disadvantages of using the drugs separately, at any rate in pulmonary disease. When one drug is used at a time, not only are resistant strains more likely to appear, thus restricting the clinical effect, but the efficacy of future treatment with combinations of drugs may be jeopardised. In patients treated with streptomycin plus P.A.S., resistance to streptomycin develops more often in those who have previously received P.A.S. alone and have P.A.S.-resistant strains in the sputum [8]: in the Medical Research Council series, after three months' treatment, 7 of 8 cultures from patients with initially P.A.S.-resistant strains were streptomycin-resistant, compared with only 1 of 4 with initially P.A.S.-sensitive strains. Similarly, in patients treated with streptomycin plus isoniazid resistance to isoniazid develops more often in those with initially streptomycin-resistant strains.[6 7] A previous Medical Research Council report [6] stated that none of the drugs should be used by itself, and that to give a combination of two drugs to a patient whose organisms are already resistant to one of them seems to be tantamount to giving the other alone and so is equally undesirable. Accordingly it was thought "essential, whenever possible, to test the drug sensitivity of a patient's organisms before a course of chemotherapy is started, so that unsuitable combinations of drugs may be avoided. . . ." But this, surely, was a counsel of perfection; for to carry out a reliable sensitivity test to all three drugs, by the methods described in our present issue, takes about two months, and there are very few cases in which it is justifiable to wait as long as this before giving the patient the benefit of the remedies. The decision to ascertain the sensitivity of the organisms before starting treatment should depend rather on the urgency of the patient's need for treatment than on the possibility of doing the test. On the other hand, routine sensitivity tests on strains isolated from untreated patients are undoubtedly very valuable for estimating the spread of resistant bacilli in a population and their threat to the public health. Hence it seems reasonable to carry out sensitivity tests on as many patients as possible, without delaying treatment for the result, and, as a guide to the choice of drugs, to rely at present on inquiry into previous antibacterial therapy. A more rapid technique of sensitivity testing would certainly be very useful. MITCHISON [9] has shown that the number of bacilli excreted in the sputum falls in the early weeks of treatment and rises again as resistance develops; and it has been suggested that these changes might help the clinician by giving him earlier intimation of the appearance of resistant strains than can be obtained from sensitivity tests.[10] The Guy's Hospital investigators, as reported in one of the two papers by them which we published last week,[11] found that the trend of counts in sputum smears was a good indication of the response of individual patients or groups to treatment, provided that the technique was uniform and the observations frequent. They suggest that in the routine control of treatment such counts are a more sensitive index of progress than sensitivity tests. But in point of fact sensitivity tests are not a measure of the patient's progress, and should not be used as such; for they do no more than indicate changes in the pattern of sensitivity of his bacilli. Though highly resistant strains are isolated, the sputum may later become free from tubercle bacilli; or the sputum may remain positive for long periods without resistant strains being detected. Thus bacillary counts and sensitivity tests are complementary rather than alternative investigations.

Patients who continue to have a positive sputum are the important group when the efficacy of different regimens is being compared. But of greater clinical interest are the much larger proportion who cease to excrete bacilli during treatment. In such cases data about the pattern of sensitivity can be obtained only by bacteriological investigation of resected lung, or of sputum from patients who relapse. BECK and

7. U.S. Public Health Service. *Amer. Rev. Tuberc.* 1953, **67**, 553.
8. Turnbull, F. W. A., Wallace, A. T., Stewart, S., Crofton, J. W. *Brit. med. J.* 1953, **i**, 1244.
9. Mitchison, D. A. *Thorax*, 1950, **5**, 144.
10. Bignall, J. R., Clegg, J. W., Crofton, J. W., Smith, B. J. D., Holt, H. T., Mitchison, D. A., Armitage, P. *Brit. med. J.* 1950, **i**, 1224.
11. Collard, P., Anderson, K., King, M. B., Chalmers, D. G., Knox, R. *Lancet*, July 25, 1953, p. 155.

YEGIAN[12] isolated tubercle bacilli from the resected lung of 9 of the 25 patients they studied. All had had antibacterial treatment for many months and 14 had a negative sputum before operation; and the only streptomycin-resistant strain found was from a patient who was known to have been originally infected with resistant bacilli. Such investigations are difficult because the tubercle bacilli found in the lesions often refuse to grow on culture media: for example, MEDLAR et al.[13] detected them in smears from 95 specimens but growth was obtained in only 26. The same difficulty has also been observed in untreated cases,[14] and it also arises in examination of the sputum: thus, of sputa seen to contain tubercle bacilli COLLARD et al.[11] found that before treatment 91% were positive on culture but during treatment only 73% were positive. Considering the great increase in pulmonary resection, there seems to have been surprisingly little bacteriological investigation of the specimens. Nor have we much information about the sensitivity of the bacilli in the sputum of patients who have relapsed. JOINER et al.[15] describe 6 cases in which the patients relapsed clinically during treatment with isoniazid and had positive sputum at the end of their course; yet ten weeks later their bacilli were still sensitive. (Further treatment with isoniazid caused improvement in 3 of them, but it was only transient.) Of 11 patients treated with streptomycin plus isoniazid, 10 had negative sputa when treatment ceased after eighteen weeks: twenty-two weeks later tubercle bacilli were found in the sputum in all but 1, and 7 improved clinically and bacteriologically when treated further with the same drugs; but the drug sensitivity of the strains is not recorded. All the patients in the Guy's Hospital trial had long-standing tuberculosis, usually with extensive, irreparable lung damage; and, if antibacterial treatment did nothing else, its reduction of the infectivity of the sputum in such cases would be of great social advantage. As the sputum commonly became positive again when the drugs were stopped, treatment of these patients for a long time—perhaps indeed for the rest of their lives—may be justified. The possibility that strains acquiring resistance to isoniazid may regain their sensitivity to it is raised again by a case of accidental wound infection of a laboratory technician with isoniazid-resistant bacilli.[16] In this case bacilli cultured from the pus twenty-one days after infection were found to be 50 times more sensitive than the infecting strain; and a similar decrease of isoniazid resistance has been recorded with repeated subculture.[17] But in the Medical Research Council trial, during the three-month period after treatment with isoniazid had stopped, there was no evidence of any general reversion either to a lower level of isoniazid resistance or to sensitivity.

We now have a mass of data about the emergence of resistant bacilli during treatment; but, as the Medical Research Council subcommittee emphasise, interpretation of the laboratory result in an individual patient is still very difficult. Patients in whom resistant bacilli have been detected may continue to improve during treatment, or, if treatment has been stopped, may respond to further antibacterial therapy. The sensitivity of bacilli in specimens of sputum obtained on different days or even on the same day may vary greatly; and the bacilli from lesions in different parts of the lung may have widely different sensitivities. Alterations in the technique of estimation may change the apparent sensitivity of a strain, and laboratories using different methods may record different results on the same culture. Hence we may conclude that though the laboratory report may warn the clinician of the presence of resistant strains which may be of clinical significance, and will indicate the combination of drugs most likely to give a favourable result, the laboratory findings do not by themselves tell us that antibacterial treatment should be stopped or that it should not be started again. The antibacterial drugs now at our disposal are highly effective in decreasing or abolishing the excretion of tubercle bacilli in the sputum. If bacterial resistance did not occur they would probably be even more effective; so it is right that the danger of resistance should be repeatedly emphasised, and that every effort should be made to prevent it. Nevertheless this danger can be exaggerated; and probably more harm is done by withholding or restricting antibacterial treatment without valid reason than by using it too much.

12. Beck, F., Yegian, D. *Amer. Rev. Tuberc.* 1953, **66**, 44.
13. Medlar, E. M., Bernstein, S., Steward, D. M. *Ibid.* 1953, **66**, 36.
14. Canetti, G. Le bacille de Koch dans la lesion tuberculeuse du poumon. Paris, 1946.
15. Joiner, C. L., MacLean, K. S., Chalmers, D. G., Anderson, K., Collard, P., King, M. B., Knox, R. *Lancet*, July 25, 1953, p. 152.
16. Borgen, L. O. *J. Oslo City Hosp.* 1953, **3**, 127.
17. Barnett, M., Bushby, S. R. M., Mitchison, D. A. *Lancet*, 1953, i, 314.

Annotations

TRENDS

THIS is a self-conscious and self-critical age. Fifty years ago a Heath Clark lecturer would hardly have chosen to speak, like Professor Mackintosh,[1] on "trends of opinion" about the public health; for the Victorians and Edwardians analysed their mistakes on a basis of what had been done, not of what had been thought about it. Yet the recognition of how dependent public policy is on public opinion is perhaps one of the best starting-points for the administrator, and he will find plenty of food for thought in this book by a man who has been medical officer of health, chief medical officer of a great department of State, dean of a famous school of public health, and professor in two universities, besides having first-hand experience of non-medical local-government administration. Professor Mackintosh's personal memories go back to the beginning of the period he is surveying, and his professional memories extend over more than half of it.

What he has to say is disquieting. He describes the great expansion of the local-authority health services in the first decade of the 20th century; the impact of the National Health Insurance Act of 1911 and the war of 1914–18; the formation of the Ministry of Health; and the passing of the Local Government Act of 1929. This Act seems to mark for him the high-water mark of local democracy in this country (though those concerned with the county districts might not agree with him) and he finds in the post-1945 trend towards centralisation and the use of non-elected ad-hoc authorities a sad decline. For reasons well supported, he does not like central Government departments and he holds that only elected bodies are strong enough and alive enough to stand out against them. But, persuasive though he is, we are still left wondering whether in actual fact an elected body is the most suitable to administer hospitals directly.

1. Trends of Opinion about the Public Health, 1901–51. By J. M. MACKINTOSH, M.D., LL.D., F.R.C.P., barrister-at-law; professor of public health in the University of London. London: Oxford University Press. 1953. Pp. 202. 12*s.* 6*d.*

With a small number of honourable exceptions, the municipal hospitals between 1929 and 1939 gave little sign of progress towards the flexibility, humanity, and diversity that are essential for the best care of the patient and the best professional work. Ten years was of course a short time for the local authorities to show what they could do in this field; but most of them seemed to be heading for rigidity, uniformity, and mediocrity. The unreformed state of local-government boundaries was not the only reason for refraining from giving control of our hospitals to the county and county-borough councils.

Some of the most interesting chapters in this book are on housing—a subject which Professor Mackintosh has made his own and about which most of us are lamentably ignorant. He has many valuable things to say about overcrowding and its effects and about the various Housing Acts. On this as other topics he writes with his customary charm and scholarship. Occasionally exasperating in his predilections, he is always stimulating and often far-seeing; and, whether one agrees or disagrees, his lectures are consistently enjoyable.

TOMOGRAPHY

A METHOD of examining radiographically separate plane sections of the body was suggested independently by Ziedses des Plantes,[1] in Holland, and by Bocage, in France, in 1921. At first little attention was paid to this technique, which was regarded as a not very important trick; and it was not until the early 1930s that tomography came into general use.

Tomography depends on the facts that a radiographic exposure need not be instantaneous and that the shadows of objects which move during an exposure are not recorded on the film. Tomographic machines and attachments are designed to secure a controlled movement between the X-ray tube, the patient, and the film while the exposure is being made. The relative movement may be obtained by shifting either the patient or the tube: it is usually more convenient to swing the tube over the patient lying on a table; but sometimes—for instance, where a horizontal body section is required—the tube remains stationary and the erect patient is rotated around a vertical axis. Twining [2] showed that an ordinary X-ray couch and tube could be suitably adapted at the cost of only a few shillings. Many different tomographic apparatuses however, have been evolved, often employing movements of great geometrical subtlety; but they differ only in minor points. It is unfortunate that different names—stratigraph, planigraph, and laminagraph—should have been given to machines so essentially similar. The common feature of all designs is a mechanical linking of the X-ray tube and film carrier; this link is pivoted, at a variable level, just above the table-top, so that during the exposure tube and film move in opposite directions along the long axis of the patient. Structures lying in the plane in which the link is pivoted will therefore be well recorded, while the projection of the overlying and underlying shadows will move and thus not appear. A good tomograph should blur out all structures lying more than 0·5 cm. from the centre of the plane (i.e., each film should represent a "cut" about 1 cm. in depth); but, because of an inevitable intrinsic blurring, small structures are not reproduced as clearly as on the plain film.

Tomography is most commonly used for examining the thorax, but it may be helpful in displaying other regions not easily accessible to plain radiography—notably, the high dorsal and upper cervical spines,[3] the temporomandibular joints, the sella turcica and other central regions of the skull, the nasopharynx, and the larynx. On the Continent the method is also used in pyelography, cholecystography, and encephalography. Tomography has long been used to detect pulmonary cavities. Nowadays, however, it is important to localise small tuberculous foci, which are sometimes treated by resection. In many cases such definition is not possible by plain postero-anterior and lateral films, and even anteroposterior tomographs do not always make clear the relation of the lesions to the fissures. Chamberlain [4] suggested that lateral tomographs could often help in this respect; and Simon [5] established that this was their most important use. He also showed that certain lesions of the middle lobe, and shadows lying below the dome of the diaphragm in the postero-anterior projection, can sometimes be more clearly seen in the lateral view. Lateral tomography should not, however, be used indiscriminately; for ordinary purposes films in the anteroposterior position are usually superior, though these may be supplemented, if necessary, by lateral views. Results are best when the examination is made by a radiologist who sees the films as they are developed, and if need be changes the projection or takes further "cuts."

It is not easy to show by tomography the fine detail of small structures casting low-contrast shadows. Lodin,[6] however, has investigated the possibility of revealing the bronchi in the lung beyond the hilum; and has demonstrated bronchi as small as 2 mm. in diameter and also detected thickening of the bronchial walls. In many cases of tuberculosis it would be extremely valuable to display the walls of bronchi beyond the range of the bronchoscope; and Lodin's method will no doubt be widely tested. Rounded foci are known to arise in at least three different ways; and though they cast identical shadows, the prognosis may be very different. To distinguish each of these lesions would be a major advance.

THE MOTHER AT WORK

ONE result of the contraction of the working week has been an increase in the demand for female labour; and plenty of women, many of them married, and with children, have been willing to accept employment. Employers have been glad to get them, for it seems that their ability to turn their hands to skilled and semi-skilled work outweighs the disadvantage of a higher absence-rate as compared with men. In a study of Glasgow mothers, Prof. Thomas Ferguson and Miss J. C. Logan [7] note that the custom of going out to work is much less well established among Scottish than among English mothers. Nevertheless the numbers in employment have doubled in the past twenty years, and this study was made to discover what influences have been operating to change family customs in this way, and what social consequences the change is having. Two groups of mothers were studied in 1951–52, between 80 and 90% in each group having one or more preschool children in the home. Where the mother went out to work, it was found, the contribution the father made to the household expenses was appreciably lower than when she stayed at home; and this held whatever the degree of skill of the husband's work. This relative parsimony with housekeeping money was thought to be a matter of policy rather than of chance.

Of the 350 mothers in jobs, 218 worked upwards of forty hours a week; and all but 48 of them had housekeeping responsibilities in addition to their work outside the home. Two-thirds of those with such household duties were working forty hours per week outside the home. Some 60% of the mothers in jobs said that they had to work to make ends meet; and an assessment of their spending-power showed that this was true. A further 30% said that though it was not absolutely necessary for them to work, the additional money allowed them

1. Ziedses des Plantes, B.G. *Acta radiol., Stockh.* 1932, **13**, 182.
2. Twining, E. W. *Brit. J. Radiol.* 1937, **10**, 112.
3. Middlemiss, J. H. *J. Fac. Radiol., Lond.* 1950, **1**, 273.
4. Chamberlain, J. M. *J. thorac. Surg.* 1950, **20**, 843.
5. Simon, F. *J. Fac. Radiol. Lond.* 1952, **4**, 77.
6. Lodin, H. *Acta radiol., Stockh.* 1953, suppl. 101. Swed. Kr. 20.
7. *Glasg. med. J.* June, 1953, p. 212.

to buy a few extras and gave them a feeling of security and independence. Most of the remainder were working with a special object—to educate a child, to buy a television set, to save enough to emigrate, or to get out of overcrowded living quarters for a part of each day. "Few were working from any real love of the work on which they were engaged."

When they came to assessing the effect on the children, Ferguson and Logan note that in Great Britain as a whole the infant mortality has fallen greatly during the present century, and—despite the increasing employment of women—is now much lower than it was even twenty years ago. Nevertheless, they found that the previous pregnancies of mothers in jobs at the time of their study had yielded a lower proportion of surviving children than the pregnancies of the mothers not then in jobs. With mothers who had worked in one or both of their two most recent pregnancies, about 27% of those pregnancies had resulted in miscarriage or stillbirth, as against 20% in mothers who had not worked during their pregnancies. Moreover, the mothers at work did not receive antenatal care as early as the others, and they had a higher incidence of premature births in their first pregnancies. Among mothers working beyond the sixth month there was a sharp increase in the proportion who did not receive antenatal care until very late in pregnancy. Nearly three-quarters of the working mothers left their jobs before the sixth month of pregnancy; but 28% of them went on beyond that time, and 10% worked on into the eighth or ninth month.

Mothers who were not at work breast-fed their babies, and continued to breast-feed them for longer periods than did mothers at work. Of the children of working mothers, 181 were looked after by a grandmother, 82 by the mother herself (in part-time work), 14 by the father (unemployed or on night staff), 24 by other relatives, 25 by neighbours, 7 by hired help, 8 by other agencies, and 4 by some combination of these; arrangements for the remaining 4 were haphazard. Among the children of mothers in jobs, gastro-enteritis was slightly more prevalent, and respiratory disease substantially commoner, than among children whose mothers stayed at home. This, of course, is merely a measure of their physical well-being: emotional malnutrition caused by separation for the greater part of the day from the mother would reveal itself only later, in behaviour disorders. The effects of such deprivation are perhaps likely to be most severe with children under two; but as we recently noted,[8] a child of three, or even of four or five, can be hampered in its development if the mother is often away. Nearly half the mothers in work complained of feeling overstrained—as they inevitably must have done if they also discharged their household duties properly. Of those employed in domestic work nearly two-thirds felt overstrained. But overstrain was not found to be most common where the hours worked outside the home were longest: rather the reverse. Mothers doing full-time work tended to make arrangements to lighten their domestic burden: many, for instance, were living with their own or their husband's parents, and could rely on these for help. Many of the mothers in part-time jobs, however, were carrying a heavy load of domestic work.

The whole picture is disquieting. Over 3 million married women are now at work in Great Britain, and nearly 40% of them are under the age of 34; most of these must have children still at school, and many will have young babies. Government policy is said to be to discourage women with children under the age of two from taking work; but economic forces act in the opposite direction. To congregate these young children in day nurseries attached to the factories where their mothers work is not a solution: it not only exposes them to increased risks of infection, but cannot undo the damage done them by separation from their mothers. It seems that the shortening of the working week has so far had the unfortunate effect of transferring part of the load from men to women, so leading women in work to do two jobs. In many cases they can only manage this by filching time which they ought to be giving to their children. National economy may benefit, but surely at a very high cost.

8. *Lancet*, 1953, i, 1137.

ASPECTS OF ENZYME RESEARCH

BIOCHEMISTRY is the youngest and most active partner in the business of experimental medicine, and of all the sciences causes the greatest unease among clinicians. It is a new language, a new set of fundamental facts, a new mental approach to human physiology and pathology, and one largely created in the last twenty years. Previously, biochemistry in medicine meant a series of laboratory aids to diagnosis—the glucose-tolerance test, the van den Bergh reaction, estimations of urinary ketosteroids, and so forth. The clinician provided the specimen, a non-medical man performed scientific manœuvres to yield some quantitative result, and from his experience the clinician interpreted the figure, without bothering very much about how it had been obtained or what were the limits of its validity. Now, thanks to the rapid progress of academic research, so much is known about the way different tissues oxidise carbohydrates or employ vitamins in their intimate metabolism that full treatment of hypoglycæmic coma or diabetic coma, of Simmonds's disease, or of liver failure demands scientific understanding, and few clinicians have the necessary biochemical knowledge. A good biochemical background is a great help, for example, in the comprehensive use of anticoagulant therapy or of endocrine preparations like cortisone, and in the employment of dimercaprol or of short-acting muscle relaxants.

It is not easy to get a quick grasp of the new knowledge. Most elementary textbooks are not modern enough or full enough to permit the student to pass straight to the latest specialised summarising article in *Physiological Reviews* or *Advances in Enzymology*, though there are one or two, like Prof. Ernest Baldwin's *Dynamic Aspects of Biochemistry*, which are helpful. The British Council therefore puts us in its debt by devoting the latest issue of the *British Medical Bulletin*[1] to enzyme research. It is not particularly easy reading, nor in 15 short articles can the whole story be told. But there are reviews of modern ideas on tissue carbohydrate metabolism and energy exchanges, on peptide synthesis by cells, and on the nucleic acids, alongside information on the fate and function of folic acid, the action of drugs on enzymes, and the significance of plasma alkaline phosphatase. Cholinesterases have assumed great importance because of their rôle in neuromuscular transmission and therefore in the effects of muscle relaxants. Their changes in demyelinating diseases, their involvement in poisoning by certain widely used spray insecticides, and their study as a guide to malnutrition or liver failure bring them into the field of practical medicine. This short review is therefore particularly valuable.

Much more, however, is needed to bring biochemistry into clinical medicine. Simpler review articles, and more of them, may help; but hospital biochemists also have a duty to enlighten their clinical colleagues directly. If the load of routine work on the laboratories could be lightened, they could teach something of the new approach, and take part in valuable clinical biochemical research, of which an enormous amount is waiting to be done. Now that there is to be money for research throughout the hospital service, clinical biochemistry should be one of the first to profit.

1. Vol. 9; no. 2.

ORAL DIURETICS

AN oral diuretic that was as effective and safe as the parenteral mercurial preparations would save much time and money. For ten years now various organic preparations of mercury have been given orally, but there is a risk of fatal poisoning, and toxic effects occur in up to 50% of patients. The most favourable report to date is that of Dimitroff et al.[1] who used an experimental organic preparation containing 10 mg. of mercury in each enteric-coated tablet. The drug was given in divided doses to a total of 60 to 100 mg. of mercury per week. Of 35 ambulant patients with chronic congestive heart-failure, 6 (17%) became intolerant to the drug, and had cramp-like abdominal pain, nausea, vomiting, diarrhœa, or an unpleasant taste in the mouth. But in the remainder the drug replaced intramuscular 'Mercuhydrin' quite effectively for periods up to eleven months. The authors stress that oral preparations are only useful in maintenance therapy when the acute phase of congestive heart-failure has been successfully treated by injected mercurials.

Since a good number of physicians are probably still sceptical about the usefulness of oral mercurials, it is encouraging to see that other fields are being skilfully explored. One of the most promising lines of study seems to be that of carbonic-anhydrase inhibitors. These agents impair renal tubular excretion of hydrogen ions and reabsorption of sodium and potassium ions. The sulphonamide group of drugs are mild carbonic-anhydrase inhibitors, and in fact Schwartz [2] has used sulphanilamide as a diuretic. The search for less toxic and more potent agents has now progressed further, and a likely drug is "compound 6063" (2-acetylamino-1, 3, 4-thiadiazole-5-sulphonamide), known as 'Diomax.' This is the preparation used by Berliner et al.[3] in their study of the relation between urinary acidification and potassium metabolism. Friedberg et al.[4] have lately described a clinical trial of this drug in patients with congestive heart-failure. Two series of patients were studied: 11 patients who required hospital treatment for uncontrolled congestive heart-failure; and 15 patients who had survived an acute episode and were able to get about on maintenance treatment. In all patients, diomax replaced parenteral mercury as a diuretic, supplementing other measures, such as rest or graded exercise, digitalis, and sodium restriction. The trial was not very strictly controlled, but the data suggest that diomax may have considerable clinical usefulness. In 9 of the 11 hospital patients clinical response to diomax was satisfactory, but the remaining 2 patients had to have parenteral mercurials. In 9 of the 15 ambulant patients diomax could be satisfactorily substituted for mercurial injections, but the other 6 patients had to return to injections. The most effective dosage of diomax was 250 to 750 mg. orally every eight hours for two to three days, during which time the excretion of water, sodium, and potassium rose and then gradually diminished to control levels. An interval of forty-eight hours or more was then required before a further diuretic response to diomax could be obtained. Alternatively, the drug could be given once daily in 250 mg. doses without tolerance developing. Mild acidosis occurred during treatment, but this did not seem to have any appreciable connection with the sodium and water loss. Only minor side-effects were encountered, the chief being drowsiness, lassitude, and paræsthesiæ in the digits, but they were never bad enough to warrant stopping the drug. The only significant changes in blood chemistry were a fall in plasma carbon dioxide content and a slight fall in pH. In those patients who did not respond to diomax, it was shown that this was not due to failure to absorb the drug from the alimentary tract. Clearly, further reports of the trials of carbonic anhydrase inhibitors will be of interest and importance.

1. Dimitroff, S. P., Thorner, M. C., Griffith, G. C. *Circulation*, 1953, **7**, 380.
2. Schwartz, W. B. *New Engl. J. Med.* 1949, **240**, 173.
3. Berliner, R. W., Kennedy, T. J. jun., Orloff, J. *Amer. J. Med.* 1951, **11**, 274.
4. Friedberg, C. K., Taymor, R., Minor, J. B., Halpern, M. *New Engl. J. Med.* 1953, **240**, 883.

NEW MENINGO-ENCEPHALITIS VIRUSES

LAST year there was an epidemic of aseptic meningitis at Port Augusta in South Australia. Most of the cases were mild; but there was one death, of a mongol child aged 13 months. From the brain of this child Miles and Dane [1] isolated a new virus which seems to have been responsible for the epidemic. The virus was recovered by inoculating an extract of the brain, cerebrospinal fluid, and meninges into cortisone-treated mice. These were used because of a report [2] that cortisone increased the susceptibility of hamsters to type-2 poliomyelitis virus; and Miles and Dane found that in mice injected with the original extract in the absence of cortisone, infection did not develop. On further passages in mice, meningitis with a mononuclear-cell reaction and myositis were produced. The Port Augusta virus is one of the larger viruses and it shares some morphological and growth characters with the viruses of the psittacosis group. Serologically, however, it is unrelated to psittacosis, mumps, and lymphocytic choriomeningitis viruses; and it is resistant to penicillin and streptomycin in ovo. Complement-fixation tests with sera from patients who had recovered from aseptic meningitis suggest that the Port Augusta virus was the cause of the epidemic.

About six months before the South Australia epidemic an outbreak of encephalitis occurred a few hundred miles further east, in the Sydney area. From samples of fæces taken in eleven cases during the course of the disease, Stanley et al.[3] isolated a hitherto undescribed virus. This virus is quite different from the Port Augusta virus, and Stanley et al. suggest including it in the Coxsackie group. Experimental infection with this virus is produced only in suckling mice less than twenty-four hours old, in which it causes a diffuse encephalitis without skeletal-muscle or pancreatic lesions. Serologically this virus, though related slightly to one of the Coxsackie-B group, has distinctive features; and Stanley et al. would place it in a new group, C. Neutralisation tests with paired sera of patients from the outbreak showed that antibodies to the Coxsackie-C virus developed early in the disease and persisted for some time afterwards.

These reports deal with the viruses isolated rather than the detailed clinical and epidemiological findings, which will be awaited with interest. Afzelius-Alm [4] investigated a series of cases of aseptic meningitis and encephalitis and recovered the viruses of mumps and herpes simplex in a small proportion of cases. In the majority of cases he recovered no virus, and most investigators have had the same experience. It will be interesting to see whether the addition of cortisone-treated mice and newly born mice to the laboratory ménage will increase the proportion of successful virus isolations.

1. Miles, J. A. R., Dane, D. M. S. *Med. J. Aust.* 1953, i, 884.
2. Schwartzman, G., Fisher, A. *J. exp. Med.* 1952, **95**, 347.
3. Stanley, N. F., Dorman, D. C., Ponsford, J. *Aust. J. exp. Biol. med. Sci.* 1953, **31**, 31.
4. Afzelius-Alm, L. *Acta med. scand.* 1951, suppl. 263.

Mr. A. A. GEMMELL has been re-elected president of the Royal College of Obstetricians and Gynæcologists for 1953–54.

Dr. G. E. VILVANDRÉ, consulting radiologist to the London Hospital, died on July 26.

Dr. MERVYN GORDON, F.R.S., died at his home at East Molesey on July 26 at the age of 81.

WE also regret to announce the death on July 26 in Edinburgh of Miss M. C. TOD, F.F.R., deputy director of the Christie Hospital, and Holt Radium Institute, Manchester.

Special Articles

THE LEGAL RESPONSIBILITY IN BLOOD-TRANSFUSION *

J. D. JAMES
M.R.C.S.

DIRECTOR, NORTH LONDON BLOOD TRANSFUSION CENTRE, NATIONAL BLOOD TRANSFUSION SERVICE

SHORTLY after I assumed the office of regional transfusion director at Barnet, an urgent-voiced doctor rang up the centre and said: "I want some blood for an emergency case quickly." He was asked: "What group?", to which he replied in a harassed tone: "Oh dear, I don't know what group this hospital is in, but I must have some blood." Another doctor telephoned the centre to elicit aid with some blood-grouping he was doing. When asked what he had so far done, he replied that he had some cells and serum mixed on a slide; adding "It has gone funny on the right—what does that mean?".

It is true that the requests we receive today show a more enlightened approach to the subject. But some clinicians and even some pathologists are still not fully alive to the hazards of blood-transfusion.

The last annual report of the Medical Defence Union mentions a considerable increase in litigation arising from transfusion mishaps; and, though this legal activity can be partly explained by the increased number of transfusions, by the fact that any Government service attracts claims for compensation, by the altered doctor-patient relationship, and by the free Legal Aid scheme, it is also partly due to an insufficient awareness of the pitfalls awaiting the unwary.

In this paper I shall begin with a brief account of the precautions taken at the North London Blood Transfusion Centre to ensure (1) that the blood the hospitals receive is of the highest standard, and (2) that the donor has not suffered as a consequence of donating—an ever-present danger in a service such as ours.

Methods

Donors are accepted between the ages of 18 and 65 years, those under 21 being required to produce a parent's or guardian's permission. In the Forces, the Commanding Officer assumes the parental rôle. The doctor in charge of the session is responsible for determining whether the donor is fit to be bled; and, as a comprehensive clinical examination is impossible he needs good clinical judgment. The doctor's handicap is somewhat reduced by the fact that the donor is required to read and answer a questionnaire containing the following list of diseases, which have been selected in the interests of both donor and recipient.

Anæmia	Nettle rash	Heart disease	Stroke
Malaria	Goitre	Consumption	High blood-pressure
Hay fever	Cancer	Epilepsy (fits)	Yellow jaundice (including contact with a case during the past 6 months)
Asthma	Diabetes	Kidney disease	

If the donor states that he has not had any of these ailments, he must append his signature. If, on the other hand, he has had any of them, he is tactfully rejected. As the National Blood Transfusion Service has decided to reject all donors with a history of infective hepatitis, it is highly advisable for anyone bleeding donors to conform with this policy lest he become involved in a case where transfusion is followed by jaundice. Except perhaps in an emergency, it is important that the donor should be screened, even though this screening is by no means foolproof.

If the donor surmounts the first hurdle, he undergoes a hæmoglobin estimation, carried out by the copper-sulphate method. A solution of specific gravity 1·052 is used, which effectively indicates those with a hæmoglobin level below 85% Haldane (100% = 14·8 g.). This method is the most suitable for our purposes, and has been independently checked by the Ministry of Health in a series of tests throughout the country. The technicians carrying out the test are visited constantly on the sessions, either by myself or some other doctor, in order to ensure that a satisfactory standard of work is maintained. Each technician's work has been checked against the Medical Research Council (M.R.C.) grey-wedge photometer for accuracy.

These donors are then provisionally grouped, using test serum of high titre and avidity.

The doctor, having accepted the donor, proceeds to clean the skin, using ether soap followed by 70% alcohol. (It has recently been suggested to me that absolute alcohol would be more effective, because dilution takes place on the skin surface; but I have not yet confirmed this.) The donor is then bled through a standard-type taking set (procaine being used as a local anæsthetic) into a M.R.C. bottle containing a standard anticoagulant. When the bleeding is complete, an elastic plaster dressing is placed over the puncture wound—but only after the donor-attendant has satisfied herself that the donor is not sensitive to such a dressing. This is temporarily covered with a pressure-bandage. The donor is then given tea and biscuits and told to rest, though occasionally some, either through lusty youth or the impatience that accompanies advancing years, refuse to do so in spite of the most dire warnings.

The autoclaving routine is carried out at our centre as follows:

Before the sets are assembled, each component is thoroughly cleaned and dried in the usual manner, and the completed sets are autoclaved at 20 lb. steam pressure for 30 min. This, in fact, is an exaggerated amount of care, since spore cultures are found to be inert after 20 min. at this pressure. At regular intervals mixed cultures, which include sporing organisms, are placed in the autoclave at the same time as the equipment, and are then sent to the Lister Institute for independent culture. Colour change tubes are also used as a further check on each autoclave run.

The water used for preparing the acid-citrate dextrose solution is obtained from stills so baffled as to produce pyrogen-free distilled water, and a sample is sent regularly to the Leeds Transfusion Centre where pyrogen testing is carried out for the whole service.

The bottles containing the acid-citrate dextrose solution are autoclaved at the same pressure for the same length of time. This produces a slight caramelisation of the glucose, which, however, is not sufficient to affect the survival of the red cells, the glucose being present in excess. The presence of caramel provides a further check that a batch has not escaped autoclaving. Recording charts are fitted to the autoclaves and filed away after each operation. Labels bearing the date and the citrate batch number and the autoclave used are stuck on the bottle so that, should any subsequent query arise, it would be possible to identify all the other bottles belonging to the batch concerned.

Before autoclaving, the aluminium cap with its perforations is covered with a brown-paper cap, which remains there until removed by the donor-attendant immediately before use. The doctor then removes the protecting tubes from the needles of the taking set and pierces the rubber wad of the bottle, which he has swabbed with spirit immediately before.

When 420 ml. of blood have been withdrawn, the needle is removed and the top of the bottle is swabbed again with spirit and the puncture holes covered with a piece of adhesive plaster. A 'Viskap,' which is carried in dilute 'Dettol' solution, is then placed over the cap and acts as a seal.

A sample bottle from each team is sent monthly to the Lister Institute for culture as a check on the efficiency of the measures employed.

* From a paper read before the Association of Clinical Pathologists, March 27, 1953.

In this way, every precaution humanly possible has been taken to ensure that the blood in the bottle has been uncontaminated. This is further assured by the fact that the teams are experienced workers in this field of medicine, and are being constantly visited during the sessions by either myself or my deputy. A further important safety factor is that fresh blood is bactericidal, so if, in spite of our régime, some organisms do in fact enter the bottle, their chance of survival, let alone multiplication, is very small. A further discouragement to their multiplication (though this does not apply to all organisms) is that the blood is stored by us at 4°C.

But the safety margin afforded by the peculiar properties of fresh blood is not present in the case of stored blood. Again, though we at the centre may have done everything possible to provide blood fit for transfusion, our responsibility lapses the moment the bottle is opened or the cap is pierced by a needle. It is even possible, in fact, to say that the centre cannot hold itself responsible once the viskap has been removed.

The Contents of the Bottle

So much for the sterility of the blood. But how do we make sure that the bottle contains the group and Rh type stated on the label?

Each time a donor is bled, a sample of blood is placed in a tube which bears the same serial number as the bottle, and this accompanies the bottle back to the laboratory.

In the laboratory the cells are checked against sera which are controlled daily for their capacity to react with A_2B cells. The serum is checked by another technician against known controlled red cells. The results are checked and correlated by a third technician. The cells are then tested against antisera C, D, and E, and a Wassermann reaction is carried out. Positive W.R. results are then sent to another laboratory for a quantitative W.R. and Kahn confirmatory test.

All this having been done, under the whole-time supervision of a pathologist, we remain conscious of the frailty of human standards; and so the label we stick on the bottle bears the phrase "Test for Compatibility before Use." Thus, finally, the onus for supplying compatible blood rests with those using it.

The controversial subject of pilot bottles has exercised the transfusion service for many years, and opinions have been sharply divided. The points in favour of a pilot bottle are obvious; those against are (1) technical and (2) legal. In my view there are *no* insurmountable technical drawbacks: in conjunction with University College Hospital, the North London Blood Transfusion Centre carried out a trial using 3000 bottles with irremovable pilot bottles attached and there was not a single case of infection or loss of agglutinability of the cells in the pilot bottle. The legal objections were described to me by a legal authority. In a case of alleged incompatible transfusion, an astute counsel could, he thought, make the point that the actual blood transfused was not tested, and that, unless the doctor taking the blood could specifically remember the actual bottle and pilot bottle in question, the testing of a separate sample was not sufficient. This is manifestly impossible in a region where each doctor may attend 400–500 donors weekly; and thus I have been unable officially to favour the use of pilot bottles. It is, however, possible that, in the near future, a solution will be found to this vexatious problem.

Training in Transfusion

The part clinicians and pathologists are taking in transfusion work raises some real difficulties. In the first place, those who are going to have charge of cases should be introduced to transfusion work either as undergraduates (in which case, a place in the medical school curriculum should be made for this study, if necessary at the expense of less potentially lethal subjects), or as postgraduates through an intimate association with the pathology department. Either course would reduce the cases in which laboratory staff are harried into providing blood at short notice, when ample time could have been given—a common cause of unsatisfactory, and therefore dangerous, cross-matching. Instruction to undergraduates would prove invaluable to them when they become doctors. A hospital blood-transfusion officer who requested packed cells from our centre, on being asked what group he wanted, replied with confidence: "All packed cells are group O." Unpopular as regulations are, it would, I think be more satisfactory if certain standards were made obligatory for those asking for blood from a hospital bank—as is done in the ordering of drugs. I believe no member of the nursing staff would be allowed to administer a drug that had not been charted by a responsible doctor; nor should she be expected or allowed to decide whether blood should be given. And yet an instance has been reported of this happening in the case of blood, with the most unfortunate results. The instructions to doctors should include a ruling that where directions from one member of the staff to another are given, they should be in written form and not verbal.

Again, if resident medical staff were better trained in blood-transfusion serology, it might have the effect of taking some of the strain off laboratory staff, who are hard-pressed these days to provide a 24-hour service. Where the laboratory is unable to give this service, is it not placing an unfair responsibility on the resident medical officer concerned to expect him to perform specialist serology without previous training? Would he not, in fact, be wise to decline to do so? Speaking as one who is Group A_2rr, I should prefer to have my blood-transfusion between the hours of 9.30 A.M. and 5 P.M. between Monday and Friday, or early on Saturday morning.

Responsibility

This brings us directly to the responsibilities born by the laboratory.

In most hospitals, the conventional arrangement in force is for a pathologist to be in charge of the hospital bank, as the one best qualified to take care of the blood; and this is the method favoured by the Ministry of Health.[1] The onus is then on the pathologist to ensure that the storage is carried out at correct temperature, and that, before issue, the blood is inspected for appearance and expiry date. These duties can be delegated to a member of the technical staff on the condition that he has been correctly trained and instructed, and is suitably supervised.

Should the negligence of a technician lead to an incompatible transfusion, the local hospital management committee, as his employer, will probably be held responsible. The pathologist in charge of the laboratory will probably not be held responsible unless there has been negligence on his own part—that is to say, improper supervision. For though the doctor actually giving the blood during a transfusion is directly responsible for the act, he is entitled to expect that, in requesting compatible blood from the laboratory, it will be provided—though he should, of course, confirm that the bottle is labelled accordingly.

Thus for other reasons besides an obvious duty to the patient, technicians in blood-transfusion serology should be constantly supervised, and each cross-matching carried out should be countersigned by a senior member of the laboratory medical staff: far from being resented by technical staff, this is usually appreciated. Moreover,

1. Use of Blood. R.H.B.(51)89, H.M.C.(51)82, B.G.(51)85.

it is not carrying precautions too far to have the technical methods employed in the laboratory, and the procedure for the issue of blood, printed and signed by the pathologist in charge, and issued to all those concerned in the laboratory. These steps proved their worth in a laboratory which had the misfortune to be connected with a fatal transfusion reaction and resulted in the exoneration of the pathologist. Similar instructions with regard to the blood-bank should be issued for the guidance of the hospital staff, and preferably pasted on the refrigerator door. Where necessary, the regional transfusion centre would be glad to assist in the framing of these instructions.

Recently, a fresh risk to the pathologist has arisen.

A regional transfusion laboratory carried out routine tests on a pregnant woman. She was found to be Rh-negative and her serum contained no anti-Rh agglutinins. The centre notified the hospital and completed a green Rh-negative card with the necessary information. This was sent to the hospital for transmission to the mother as usual. The mother became pregnant again some time later and was delivered of an erythroblastotic baby by cæsarean section. This baby died, despite replacement transfusion. Subsequently the mother became aware of the fact that the green card had not been sent to her; in fact it was discovered attached to the hospital case-notes and given to the mother after the second pregnancy. Alleging that, had she known that she was Rh-negative, she would not have essayed a further pregnancy, she took legal advice and instituted proceedings.

Conclusion

Blood-transfusion work has forced itself like an unwelcome visitor into the cloistered calm of the pathological laboratory—but it is a visitor that must not be ignored. Indeed it must be treated with respect; for though the director of a pathology department may be wedded to the histology tray or the burette, he should be guided by discretion, if by no other motive, into becoming thoroughly conversant with a technique which (unlike almost any other technique carried out in a laboratory) can lead to the death of the patient.

But whoever is legally responsible at various stages in the channel from donor to recipient, it is a comforting thought that, if we all carry out our professional responsibility to the patient to the best of our ability, and exercise due care and skill in our work, we can do no more, and the question of legal responsibility assumes a lesser degree of importance.

FIRST INTERNATIONAL CONGRESS ON MEDICAL LIBRARIANSHIP

OVER 300 medical librarians, from places as far apart as Canada and Thailand, Spain and Yugoslavia, attended this congress held in London from July 20 to 25 under the presidency of Sir CECIL WAKELEY, F.R.C.S. The members were entertained at receptions and parties at the Royal College of Physicians, the Royal College of Surgeons, Apothecaries' Hall, the Royal Society of Medicine, the British Medical Association, the Ciba Foundation, and the Wellcome Research Institution. An exhibition of medical periodicals of the world was held at B.M.A. House, and the American Military Attaché opened the Armed Forces Medical Library Exhibition at the Wellcome Research Institution. At the last session of the congress a committee was set up to plan the second congress.

Opening the congress, Sir CECIL WAKELEY said that, as a practising surgeon, he had long known that some of the finest consultants available were to be found in the medical libraries. He explained that he was referring not only to the volumes on the shelves but also to those living guides to knowledge—the medical librarians.

CENTRALISATION

Mr. W. R. LE FANU (Royal College of Surgeons of England, London), in a survey of the medical libraries of Britain, said that the University of London was beginning to form a medical collection which might ultimately become a central medical library for the postgraduate and undergraduate schools of the university. The development of the London medical-school libraries, formerly very unequal, had been encouraged by the University Grants Committee; each now employed a trained librarian. Under the National Health Service the creation of libraries for qualified and auxiliary staff and for nurses had been set as a goal for all hospitals. The library of the National Institute for Medical Research acted as a clearing-house for information and for inter-library loans. The medical section of the Library Association had organised an exchange service for duplicate material, through the Wellcome Historical Medical Library.

Mr. F. N. L. POYNTER (Wellcome Historical Medical Library, London) had worked out that the 48 medical libraries in London together took 11,000 periodical subscriptions each year. The storage of bound volumes was a problem. Why not, he suggested, assemble in one spot all medical periodicals that were seldom consulted? Some medical libraries also possessed collections of old books which were allowed to remain purely for sentimental reasons. There was a good deal to be said for collecting them in one place, where they could be consulted by scholars and where there was a specialist staff. A depository for historical texts was also advocated by Miss GERTRUDE ANNAN (New York Academy of Medicine Library).

CATALOGUING

Lieut.-Colonel FRANK B. ROGERS, M.D. (Armed Forces Medical Library, Washington), pointed out that, though his library (formerly known as the Surgeon-General's Library) had abandoned the *Index-Catalogue*, it had not abandoned its responsibilities to bibliography and medical librarianship. The *Current List of Medical Literature* appeared monthly; presently it would do so with semi-annual cumulations. The annual *Armed Forces Medical Library Catalog* dealt with monographs and serial titles, and occasional special bibliographies were published on topics of current interest—for example, A.C.T.H. and cortisone, and, most recently, military neuropsychiatry.

Miss HELEN BAYNE (New York University/Bellevue Medical Center) and Miss ILSE BRY (New York Psychoanalytic Institute) described how, in 1950, a group of librarians in charge of psychiatric and psychological collections in America started to sort out the material published in these subjects, much of which is at present unknown because it is buried in periodicals. This modest, wholly unfinanced, beginning of the Psychoanalytic Collections Conference of New York had to be limited, but they would like to extend the work.

Dr. MASAO WADA (Tohoku University, Japan) regretted the high cost of medical periodicals.

Mr. H. A. IZANT (W.H.O. Library and Reference Section) said that his section scrutinised current periodicals, indexed relevant articles, and supplied bibliographies, reference lists, and photocopies. It was also preparing future editions of *World Medical Periodicals* and a series of guides in English and French to medical literature.

Mr. EDWARD CARTER (Libraries Division of UNESCO) described the international exchanges of publications and other projects of his organisation, such as help for the Medical Faculty Library at Tehran.

The Wider World

IN ANTARCTIC WATERS

F. K. M. HILLENBRAND
M.D. Rostock
MEDICAL OFFICER, FALKLAND ISLANDS

MANY a visitor to the Natural History Museum at Kensington must have stood in awe before the gigantic blue whale which, with other curios displayed in the same gallery, conveys some of the "atmosphere" of the far-off South Atlantic.

There are no regular shipping lines to these waters, and even nowadays the voyage takes up to six weeks or more—long enough for acclimatisation. Some time before albatrosses herald the proximity of Southern latitudes, large reddish-brown patches on the surface of the water indicate *krill* (shrimps), which apart from zooplankton is the large rorquals' main food. Through the gales of the Roaring Forties the ship ploughs its way southwards, until on the last stretch of the voyage the weather becomes calmer; and now a thick fog appears and conveniently hides from the unsuspecting traveller the numerous icebergs which surround South Georgia throughout the year.

* * *

South Georgia is the northernmost island of the scattered archipelago which extends from Graham Land in the west to the South Sandwich Islands in the east. All these islands are situated in a hairpin-shaped area, the Scotia Arc, thought to be a submerged continuation of the Andes, of which the islands are the very mountain tops (fig. 1). They may well have been volcanoes in ages past, and subterranean warmth is considerable at some of the shores, although there are no warm oceanic currents.

This part of Antarctica has been the scene of countless human endeavours, from the 16th century onwards, when navigators touched its outskirts searching for the South-west Passage, down to Shackleton's memorable expeditions. Not for nothing was *Resolution* the name of the ship which carried Captain James Cook on the voyage when he discovered South Georgia in 1775. He took possession in the name of King George III, after whom he named the island; but he was disappointed at having discovered another island instead of the Southern Continent he expected but never found, and his companion Anders Sparrman, a Swedish naturalist, sadly declared it worth less than an English cottage. Nevertheless, his discovery opened up the area. In his wake, fur-sealing, then sealing for the blubber of elephant seal, and eventually whaling, led to the exploitation of the riches of Antarctica which continues to this day. There is also some mineral wealth in the region, copper as well as coal having been found; but no mining is done.

Antarctica is the world's largest resource in animal fat. Rorqual oil is readily convertible into edible fat, and is nowadays a necessity for the margarine and cosmetic industries. In 1951 the United Kingdom received over 123,000 tons of whale oil; but frozen whale-meat did not seem to find a market in Britain, though it tastes all right when eaten "on the spot" in 64°S., and after being smoked it closely resembles smoked salmon. So far as quantity goes, the thought of 300,000 liberal helpings of "roast beef" from one blue whale should, one would think, allure the British housewife. Then there are the by-products: bone and meat meal find a ready market as cattle food and fertilisers, and recently trials have been made with concentrated extracts from glue water, and a mysterious preparation furthering growth and marked A.P.F. promises chickens and turkeys of gigantic size. The baleen (whale-bone) is now thrown "over the side" because corsets are no longer fashionable. (Myriads of Cape pigeons, the scavengers of the Antarctic Ocean, feed on the refuse of whale processing.) Ambergris, the toothed sperm whale's peculiar inflammatory intestinal product, is no longer coveted for the perfume industry, in which it has been replaced by synthetic fixatives. Sperm oil, however, from the large skull cavity, still fetches a high price, being now used for wax preparations, and washing and emulsion powders. The high content of vitamin D in whale oil has long since attracted the pharmaceutical industry, but there seems to be still a future in utilising various glands for organotherapy, provided the commercial approach to "whale oil only" can be overcome. A promising start was made in 1951, when 185 kg. of whale pituitaries (from about 9000 whales) was collected for the production of A.C.T.H.

* * *

The arrival at South Georgia introduces a new world which in its contrasting qualities is both fascinating and repulsive. Old-world hospitality greets the newcomer at the whaling station ashore. He needs it, too, after a first informative walk round the station. The sight of the *flensing plan*, where the whales are cut up, is revolting and the smell from the oil cookeries sickening. The stench of a whaling station during the fishing season impregnates clothes and body, and is as little avoidable as the all-day topic of conversation which reminds you that this is the world's largest whaling centre. Bare rocks, and narrow shores with a sparse vegetation of tussock-grass and a few mosses, are set against a background of glaciers which in their grandeur are reminiscent of the Alps. There is veritable alpen-glow, and unforgettable sunrises and sunsets with colourings in all pastel shades, if the day is fine; but there are avalanches too, and landslides. The fine harbours of South Georgia are in winter occasionally blocked by drifting icebergs, which are dangerous to the ships moored there. Now and then zoologists and photographers of note visit the island, which has a rich indigenous fauna, both beast and bird. In addition, reindeer were imported from Lapland early this century and have taken to the island almost as well as the brown rat, which, originally a stowaway from the sailing ships, has now developed a long fur suited to the climate. In winter, when work is slack, there are opportunities for hunting shags, reindeer, and leopard seal.

South Georgia possesses the southernmost church in the world; but since the mid-'30s it has not been used as a place of worship, and it now serves as a library.

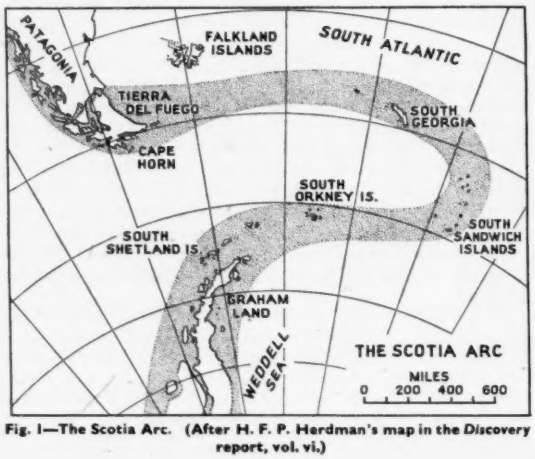

Fig. 1—The Scotia Arc. (After H. F. P. Herdman's map in the *Discovery* report, vol. vi.)

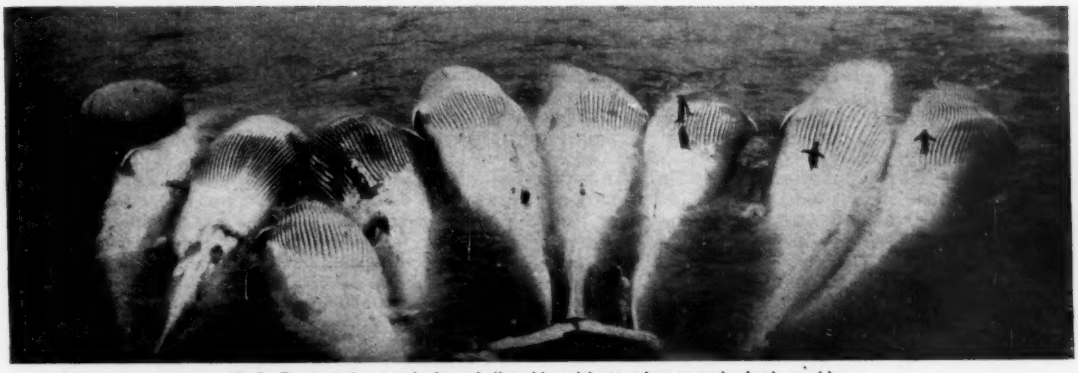

Fig. 2—Dead whales attached to whaling ship, with attendant penguins having a ride.

During the Antarctic summer, some 1200 men work on South Georgia's three whaling stations, and in winter about half this number carry out ship repairs in the dockyards, maintenance work on huts, workshops, and whaling gear, and, to a small extent, process blubber from elephant seal. Now and then transport vessels call, and at the beginning of the new whaling season some of the floating factories call at the island before going further south for pelagic whaling. With their flotillas of a dozen or more catching vessels and a complement of some 600 men, they operate independently of the land stations. The speedy catchers are equipped with wireless, radiotelephone, radar, and echolot. The factories, of 20,000 tons or more, represent the neplus-ultra of modern whaling, and are capable of disposing of a record catch of 63 whales within little over twenty-four hours. The coming of the industrial revolution in whaling was marked by the invention in the '90s of the last century of the harpoon with an explosive head. The harpooner of old is now a gunner, duly organised in a Gunners' Union.

The skill of these men is remarkable, but the efficiency of the industry has not yet resulted in developing more humane methods of killing. The activities of UFAW (the Universities Federation for Animal Welfare) have at last led to trials of an electric harpoon, and experiments with carbon dioxide, the gas harpoon, have been made in order to shorten the agony of the whale. Unless hit in a vital spot, a whale wounded by the explosive harpoon takes 20 minutes to die, and it is said that whales do not even develop wound shock which would relieve their pain. Often enough, more than one harpoon is needed for the coup de grâce.

International regulations limit whaling as to size, type, and species, as well as to time and region. Guided by scientific observations on the migration of whales and on stocktaking, the aim is to avoid the mistakes of the past and to preserve the world's largest mammal. Nevertheless, to the outside observer, the number of rorquals killed annually under the present agreement seems very high. Moreover, the very large number of female whales in advanced pregnancy which are killed at the height of the season raises the question whether the industry is not undermining its own foundation. The killing of a whale in milk is an appalling sight; but, however great the gunner's skill, it cannot be prevented, unless he chances to see the second very small spout.

* * *

The climate of Antarctica is rigorous, and up to fifty years ago it was thought impossible to live there for any length of time. Since then, several whaling stations, and later bases for meteorologists and geologists have been established and have been occupied continuously for years by the same men. Even some few women and one or two children live in South Georgia without any obvious adverse effects on their health. Chilblains are almost unknown, and respiratory diseases, besides being very rare, seem to clear up quicker than elsewhere. The length of the voyage may be the reason why the infectious fevers are as yet scarce in Antarctica. Common colds, however, occur with great regularity a few days after the arrival of ships, and men who have been in the region for a long time contract them sooner than the newcomers. At the bases, ascorbic-acid tablets and orange juice supplement the diet when fresh food from animal sources, such as seal liver, penguin breast, or penguin eggs, is not available; at the whaling stations the fare is rich in protein, and, besides salted meat and fish, fresh meat from whales, cormorants, and reindeer is eaten. The old South Georgian habit of eating the antiscorbutic tussock-grass has been abandoned, and vegetables are imported, though they often have to be stored for a long time. I saw no nutritional deficiencies apart from one severe case of scurvy in a young man who during his nine months' stay in the region had by his own choice lived almost entirely on tinned food, salt meat, and salt fish.

Atmospheric conditions vary greatly within the region. In South Georgia, with its almost Alpine character, sensitive people sometimes react to a sudden fall of barometric pressure by having stenocardiac attacks. Similarly, frequent atmospheric changes, blizzards, and the absence of any sunshine on the largest station for four months of the year, together with the psychological effects of isolation, may, in predisposed persons, be the cause of depression, claustrophobia, and melancholy.

* * *

Whaling and sealing give rise to a number of conditions peculiar to these occupations. The handling of steel ropes on the *flensing plans*, and the cutting up or mere handling of the carcases, cause troublesome infection of small, mostly superficial, cuts or scratches of the hands and fingers. Sometimes also the knives used for flensing the whales, razor-sharp and shaped like hockey-sticks, are responsible for injuries to tendons—perhaps more often on the "floating factories" where the piece-work system results in a rush and bustle which favours accidents. A mild form of gastritis with constipation is often seen when the shifts and meal-times are changed half-way through the season. The men call this condition "shifting pains." A characteristic conjunctivitis is seen in men working with refining apparatus (separators) which emit whale-oil fumes. Caustic burns to the eyes and hands are often caused when the ship is sprayed with caustic soda at the end of the whaling season. Odd injuries sometimes occur on warm midsummer days, when melting icicles—three feet or more in length—suddenly drop from the derricks or masts on to the deck. Insufficiently refined sperm-whale oil, a popular remedy

for rheumatic complaints among whalers, and soap made from rancid whale oil and used for their laundry, not uncommonly produce dermatitis.

A number of conditions which also occur elsewhere are encountered here more often. Acne is frequently seen, especially on the factory ships, where the daily fare is very rich in proteins. In South Georgia, skiing in winter and football in summer supply the injuries associated with these sports. The men usually smoke a great deal, tobacco being very cheap; and the opponents of nicotine abuse may claim support for their theories in the fact that many young men have hypertension. The work in dockyards, in workshops, and on ships leads to a variety of accidents no different from those occurring in similar industries at home, though the covering of ice on the deck of a whale-catcher adds to the risks. Surgical emergencies are rare, but the doctor confronted with them usually has to rely wholly on his own resources. Even in South Georgia, where there are at least two doctors during the winter, the lack of any sort of road, and the gales at sea, usually prevent medical consultation.

* * *

Civilisation has alleviated the rigours of the Antarctic, and life there today bears little resemblance to the picture an old Norwegian salt may draw of days not so far away. Still, despite radar, the approach to these coasts is formidable even to the experienced navigator, and life in these icy wastes is full of hardships for body and soul. It is, therefore, the hardy type of men, with a spirit of adventure handed down from ancestors who roamed the seas—men from the Scottish mainland, from the Shetlands, and from Norway—who lead their lonely life here, separated from their families. They help to provide a substantial part of the basic requirements for millions at home. Their attitude towards work, and their mentality, are such as to prevent their seeking medical advice unless they really need it. To be a doctor among these hard-working people has been a great experience, and a privilege.

Graham Land, protruding from the Antarctic continent like a finger, beckons to the men from the north. Today as strong as ever they feel this strange "call of the south" to the area which has witnessed the epics and endeavours of men like Scott, Shackleton, and Bruce.

Public Health

SLUM CLEARANCE AT SEA 1936–53 *

J. GREENWOOD WILSON
M.D. Lond., F.R.C.P.
MEDICAL OFFICER OF HEALTH, CITY AND PORT OF CARDIFF

> "OF late, many shipowners on their own initiative have taken an active interest in the conditions of life on board their vessels, and are endeavouring to render the lives of the men employed more healthy and comfortable. . . . It is to be hoped that this improvement will extend and embrace all classes of vessels, and there is no doubt that the lives of the men will thus be prolonged, the hardships incidental to their calling in many ways ameliorated and the service made more attractive."

These words were written in 1916 by Dr. William Hanna, assistant port medical officer for Liverpool, and ever since its inception in 1898 the Association of Sea and Air Port Health Authorities has been active in promoting his hopes. They have bombarded the interests concerned with letters, memoranda, and requests for reception of deputations (some of which have been granted!). In 1922 and again in 1935 the association published *Recommendations*, most of which were incorporated in the 1937 Board of Trade *Instructions to Surveyors* on the construction of living-quarters for masters and crews in new merchant ships. The main improvements suggested were in ventilation and lighting, and in the provision of central heating, drying-rooms, heated washplaces, separate messrooms, oilskin lockers, individual metal wardrobes and food-lockers, and proper water-closets.

At the annual meeting of the association in 1936 I compared the living and working conditions of workers at sea and ashore, and pointed out how unfavourable conditions were reflected in the health (particularly tuberculosis) statistics of the seafarer.[1] It now seems opportune to see how conditions at sea have improved since then.

Yesterday

Originally, the foc's'le came to be known as the living-quarters of the crew because by tradition they lived in the forecastle space in the bow of the ship. Not only was this the most dangerous spot in a collision or in stormy weather, but it entailed hazardous journeys to and from the other parts of the ship, particularly for food and hot water. In the old cargo vessels all entrances to the foc's'le were exposed to the weather. To the port and starboard a small compartment with a metal trough served as a water-closet. The trough was flushed when the deck water service was in operation. The same compartment was often used as a substitute for a bathroom. A separate bathroom or washroom was not generally provided. Each man was provided with a bucket, not necessarily a new one, as a bathing utensil and he procured warm water from any source he could find. Sometimes he bathed in the foc's'le, sometimes in the stokehold or on the open deck.

In these spaces of triangular form, the sailors and firemen slept, fed, washed clothes, sometimes washed or bathed themselves, and spent their limited recreation. Natural light, which found its way through a few small port-holes, was restricted by two-tier bunks and was totally inadequate in distribution. Men who occupied the inboard two-tier bunks were often in semi-darkness. No provision was made for hanging up clothes, whether underwear or overcoat, with the result that lines were improvised between bunk stanchions and further obscured the light. Artificial lighting was inadequate, depending mainly on oil lamps. Electric points were supplied but were seldom used.

Heating was usually provided by an enclosed stove and flue-pipe. No coal-bunker was supplied and there was seldom a proper ashes collector. Because the space was limited, the stove had to be placed in a position near somebody's bunk with consequent discomforts—fumes, dust, smoke, overheating, and disturbance. Occasionally radiators, fed with steam from the deck-machinery lines, were used. But all other demands took priority, and the supply of steam was irregular, owing to steam-pipe repairs, shutting down boilers at the end of the working day, condensation in long deck-pipes, &c. The installation was invariably neglected and for one reason or another, it was often impossible to shut off the steam in hot weather.

Ventilation was by flange coamings and cowl ventilators, providing about 3 sq. in. for inlet and a similar area for outlet of air per man. In bad weather, which would often last for days, these ventilators would have to be unshipped and the vent coamings securely plugged to avoid flooding of the foc's'les. The steel plating of the bows and deckhead without external insulation were generally coated internally with cork-dust which had become ineffective through successive coatings of oil-

* The substance of a paper read at the annual meeting of the Association of Sea and Air Port Health Authorities, Sunderland, June 17–19, 1953.

1. Wilson, J. G. *Lancet*, 1936, ii, 645.

bound paint. The quarters were thus exposed to the heat of tropical sun and excessive condensation in winter.

A battery unit of small wooden lockers rested in some convenient spot. One locker, perhaps 2 × 1 × 1 ft., was allocated to each man, in which he was expected to store his personal belongings and ration of foodstuffs. In some of the older ships there were not even clothes lockers, and the men had to keep their clothes in their sea-bags during the whole voyage. Neither bed nor bedding was provided and it was a common sight to see seamen humping their straw palliasses or "donkey's breakfast" on their backs when joining ship. Wooden bunks and partition bulkheads, usually of the tongue-and-groove type, were ideal harbourage for bugs and other insect vermin.

In the middle of the foc's'le stood a large bench-table and wooden forms alongside the tiers of bunks. This further cramped the quarters and it was the only place where the men of one watch could eat or enjoy recreation, such as card playing, while the other watch were trying to sleep in the bunks beside them.

All water and food had to be carried from amidships to the foc's'le and in bad weather, with decks awash, this was a perilous feat which meant a certain drenching. Hence the food usually arrived on the table in a cold, soggy condition.

Today

So much for the dark picture, but what of modern conditions?

Accommodation is now situated in the stern or amidships; this is designed to give comfort with privacy, and where possible each man is allocated a single-berth cabin with the entrance protected from the weather. The port-holes are bigger and cabin furnishing is arranged to admit as much daylight as possible. A generous supply of electric lighting is available by day and night, and it is common to find a bed-head light for each bunk.

Mechanical ventilation from properly controlled units is steadily replacing the natural ventilator. In the better planned quarters the provision-room ventilation is separate from the main scheme. Portable electric fans are sometimes supplied for tropical climates. The mechanical ventilation scheme which supplies air at a predetermined temperature helps considerably. This is sometimes supplemented by a centrally heated low-pressure hot-water system or a steam-heater coupled to a major source of heat such as the ship's boiler.

It is now a recognised practice to provide a specific messroom or a number of messrooms according to the size of the crew, for petty officers and ratings of each department and to locate them as near the galley as convenient. Adequate fittings are provided for feeding, warming food, boiling water, storing equipment, and washing up. Sometimes there is a refrigerator-larder. Many ships now have well-equipped recreation-rooms where those who are off-duty can play games without disturbing the privacy and rest of others.

In w.c.s only porcelain wash-down pedestals are now fitted, and these are contained in cubicles with a reasonable degree of privacy. The pedestals have cut-away seats and a consistent supply of piped flushing water. The compartments are constructed with impervious surfaces and deck-scupper drainage. A separate compartment for washing and bathing with impervious surfaces and a drained deck are usual. It is suitably lighted, heated, and ventilated, and equipped with stoneware wash-basins and shower-baths, and often has facilities for washing clothes. Hot and cold running water is generally on tap. For drying clothes there is a warm and ventilated compartment with hanging facilities, and usually there are special lockers for dirty clothes and oilskins.

Furnishing and decoration of living-quarters is much improved and condensation is avoided by better insulation. All necessary measures are taken to avoid harbourage of insects or dirt, and the provision by shipowners of mattresses, often of rubber latex, in place of the old "donkey's breakfast" or straw mattress, has done more than any other measure to counter verminous infestation. The bedding includes good covers for mattress and pillow and a set of linen, with possibly a counterpane as well. The linen is changed regularly.

All cabins are fitted with a metal frame cot or hardwood bunk for each occupant and there may also be a settee which obviates the need to sit about on the bunk. Some ratings' cabins nowadays are fitted with chests of drawers, concealed writing-tables, chairs, wardrobes, curtains, and foot rugs. Exceptionally a wash-basin with hot and cold fresh water is also included. A mirror is almost always provided.

When everything possible has been done to improve the construction of crews' quarters, there still remains the obligation on the men themselves to keep their quarters clean and tidy, an obligation which is not always well fulfilled. Efforts have been made—e.g., through the National Maritime Board agreements—to see that this is done, but not yet with complete success. A few shipping lines, it is believed, seek to short-cut this difficulty by employing mess orderlies to keep the quarters clean, though even here the arrangement tends to fail at paying-off ports.

Some Points for the Future

Accommodation for food storage has not improved as much as living conditions, and many of the old criticisms still hold good. The association will, no doubt, still be mindful of its efforts to secure powers of inspection of ships foodstuffs by port health inspectors—powers which are still opposed by the Ministry of Transport. It is probably still the view of the association that this opposition is unreasonable and savours of a vested interest.

Another recommendation of the association which has not yet widely been adopted is the suggestion to employ sick-bay stewards, who could find plenty to do on big ships as health educators, in taking care of anti-mosquito precautions, and in helping with medical examinations, inoculations, and the treatment of venereal disease.

Nor has the association's recommendation for better health and welfare services for the seamen ashore received much attention. The association suggested the provision of seamen's baths, hostels, and clubs, and prompt and adequate medical attention at the docks, like that offered to dock labourers under the scheme of the National Dock Labour Board—though it is sometimes claimed that this is adequately provided at large ports by the Shipping Federation Medical Service. Last, but not least, such welfare and medical schemes for the seafarer should certainly include arrangements for aftercare and rehabilitation which are at present neglected.

When all has been said and done, however, there can be no doubt that there has been a vast improvement in the lot of the seaman, an improvement which is reflected in the available health statistics.

In 1936 the incidence of tuberculosis in the Royal Navy was high—comparable to that of the Merchant Navy. Though in the ships of the Mercantile Marine there was competition for space and amenities between human and other cargo, in the ships of the Royal Navy human needs had to be balanced against the requirements of what is essentially a floating fighting machine. Since the late war a great deal of scientific work has been carried out by the Royal Navy Personnel Research Committee (a committee of the Medical Research Council) on the effect of adverse environmental conditions upon the health and working efficiency of naval personnel. These investigations continue and are being borne in mind when designing new ships and refitting old ones.

Considerable attention has been paid to the improvement of ventilation systems. During the war years it was not possible to compile health statistics on the Navy, and though they have recently been restarted, it is too early yet to show statistical evidence that these measures have improved the health of the sailor.

One arrangement which I consider to be of great importance for Naval personnel is that all officers and men are now examined annually with X rays. Whatever may, or may not be done for the improvement of living accommodation on board ship, it is obvious that a great advance in early diagnosis, with consequent reduction of the incidence of tuberculosis, would be achieved if all officers and men of the Merchant Navy were also radiographed annually. Measures of this kind remind us that in concentrating upon better conditions afloat we must not overlook the corresponding need for adequate medical, public-health, including housing, and welfare services, for the seafarer ashore.

In 1936 I asked you to come with me to sea to look for yourselves at the seamen's living and working conditions on board ship. Today I ask you to disembark and see what needs to be done to help the seaman get his land legs; for it seems now to be ashore, rather than at sea, that we should look most searchingly for adverse factors in the seaman's environment.

I am obliged to the port medical officers of Bristol, Kingston-upon-Hull, Liverpool, London, Manchester, Middlesbrough, Sunderland, and Swansea for information and comment, also the medical officers of health of Manchester, Newcastle upon Tyne, and South Shields. In addition, the port medical officers of Bristol and London sent me graphic accounts of crews' quarters "then" and "now" upon which I drew freely, and the port medical officer of London went out of his way to encourage me to proceed with this paper.

Poliomyelitis

Poliomyelitis notifications (uncorrected) in the week ended July 18 (the 28th week of the year) were (previous week in parentheses): paralytic, 147 (118); non-paralytic, 76 (65); total, 223 (183).

The following table compares this year with the preceding six years:

Year	Total cases up to and including 28th week	Cases in 28th week
1947	613	126
1948	746	38
1949	748	117
1950	1659	212
1951	1027	120
1952	1014	119
1953	1423	223

For the week ended July 25 the provisional total is 266 (paralytic, 152; non-paralytic, 114).

Food-poisoning in the London Area

In the past few weeks there have been several outbreaks of food-poisoning in the London area, and there is now evidence that the cause was a consignment of dried milk that had become contaminated with staphylococci. The Ministry of Food has warned schools, hospitals, and other institutions in the Home Counties that they should not, for the time being, use dried milk from tins bearing the code letters T.V.D.[1] The suspected milk was a consignment made for distribution by the Ministry of Food, and it is not on sale to the public by retailers. This milk is thought to have been responsible for the outbreaks at schools in Ewell, Surrey, on June 27 (when about 100 cases were reported), Banstead on July 8 (about 50 cases), Epsom on July 9 (207), Richmond on July 10 (93),[2] Battersea on July 17 (102), Paddington on July 17 (33), and Camberwell on July 24 (137). A total of rather more than 700 people, most of them school-children, have been infected in these outbreaks. Staphylococci have been isolated from opened tins used to prepare school meals and from unopened tins from the same stock. The earlier outbreaks seemed to be the result of using the milk for cold foods—e.g., synthetic cream and chocolate fillings—but at Battersea it had been heated in the preparation of custard. In feeding tests, volunteers suffered no ill effects from drinking milk freshly prepared from suspected tins, suggesting that the milk became harmful only if it had been allowed to stand for some time after reconstituting. The investigation is continuing.

1. *Times*, July 25, 1953.
2. See *Lancet*, July 18, 1953, p. 144.

Contaminated Frozen Food

In a case before the Court of Appeal,[1] a Liverpool firm, dealing in frozen foods, appealed against the dismissal of the claim that they had brought against the foodstuff importers who had supplied them with a contaminated consignment of frozen precooked ham and eggs. Almost the whole consignment had been destroyed, as unfit for human consumption, by order of a magistrate. It was stated that the food was contaminated by pathogenic staphylococci, but that there was no risk of infection provided it was eaten within twenty-four hours of its removal from cold storage. Counsel for the defendants claimed that there was no evidence that the organisms were harmful by mouth. During the hearing, it was said that as a result of this case the Ministry of Food might insist on labels being put on these foods, stating that they should be eaten within twenty-four hours. Lord Justice Denning remarked that it was not well known in this country that frozen foods should be eaten within this time, and the fact should be publicised. The appeal was allowed.

Second Quarter in England and Wales

The Registrar-General[2] announces the following provisional figures for England and Wales in the quarter ended June 30 this year (corresponding figures for the same quarter last year in parentheses): birth-rate 16·4 (15·9) per 1000 population; stillbirth-rate 22·9 (22·4) per 1000 total live and still births; death-rate 10·5 (10·6) per 1000 population; and infant-mortality rate 25·6 (25·1) per 1000 related live births.

First Quarter In Eire

In Eire during the first quarter of this year,[3] the birth-rate was 21·3 per 1000 population, which was 0·5 below the rate for the first quarter of 1952. The equivalent annual rate for the number of deaths in the quarter was 14·3 per 1000 population, being 0·1 below that for the first quarter of the preceding year. The death-rate from all forms of tuberculosis was 0·5 per 1000 population (respiratory 0·4, other forms 0·1), compared with 0·6 (0·5 and 0·1) in the same quarter of 1952. The maternal-mortality rate was 1·3 per 1000 births registered, compared with 1·2 in the corresponding quarter of 1952. The infant-mortality rate was 44 per 1000 births registered, as against 55 in the March quarter of 1952.

1. *Times*, July 23, 24, and 25, 1953.
2. Registrar-General's return for the week ended July 18. H.M. Stationery Office. Pp. 20. 1*s*.
3. Quarterly Return of the Marriages, Births, and Deaths. Obtainable from the Government Publications Sale Office, G.P.O. Arcade, Dublin. Pp. 15. 6*d*.

Parliament

QUESTION TIME

Examination of Recruits

Mr. N. N. DODDS asked the Minister of Labour if he would hold an inquiry into the present medical board system operated by his department to restore public confidence in this important Government machinery concerned with recruitment to the Services.—Sir WALTER MONCKTON replied: No, Sir. I am now engaged on the consultations with chairmen of medical boards. I have already arranged for the boards to be reminded of the importance of making a full inquiry into the candidate's medical history and of paying full attention to consultants' reports. I propose, with the coöperation of the Services and the Ministry of Pensions, to investigate all cases of men discharged during a recent period shortly after entry with a view to determining the present extent of error and whether it appears to arise most commonly in certain types of cases or districts.

Replying to further questions, Sir WALTER MONCKTON said that he was anxious to do all he could to probe this

matter, because, although it was easy to say that the cases which came to his notice were few against the quarter of a million examined in a year, if there was one case he would like to track it down. He would certainly consider the suggestion that psychiatrists should be in attendance on local medical boards. Arrangements were already in hand to include in the call-up notice a statement that certificates from private doctors submitted on reporting for medical examination would be taken into consideration by the medical board. These revised call-up notices were to be put into use as soon as they were printed. The amendment was in these terms:

"The Medical Board will give careful consideration to any medical evidence which you may bring with you regarding any illnesses or disabilities from which you have suffered."

Committee on Air Pollution

Replying to questions, Mr. A. E. MARPLES, parliamentary secretary to the Ministry of Housing and Local Government, said that the terms of reference of the committee which was being appointed jointly by the Secretary of State for Scotland and the Minister of Fuel and Power were:

"To examine the nature, causes and effects of air pollution, and the efficacy of present preventive measures; to consider what further preventive measures are practicable; and to make recommendations."

The 11 members of the committee include Dr. J. L. Burn and Prof. T. Ferguson, M.D. The chairman is Sir Hugh Beaver, M.INST. C.E.

Army Psychiatric Reports

Mr. MICHAEL STEWART asked the Secretary of State for War to what persons, and for what purposes, the contents of Army medical or psychiatric reports might be disclosed.—Mr. A. H. HEAD said: The general practice of the War Office is not to disclose the contents of Army medical records, including psychiatric reports: they are regarded as a confidential class of document for which privilege is claimed as a class. The department will, however, exceptionally waive the claim to privilege, if necessary in the overriding interests of justice, in serious criminal cases and is prepared, in such cases, to make the records available both to the prosecution and the defence. Medical records of ex-Service personnel may also be disclosed, with their agreement in each case, to doctors to assist in treatment. Certain parts of a military psychiatrist's special report on the accused, but not other medical records, may be made available in confidence to the prosecution and defence at a military court-martial, to assist them in the conduct of their cases; and portions relating to character may be produced to the court in mitigation of sentence if the accused is convicted.

I understand that some parts of a psychiatric report dated May 6, 1953, on Private Irene Rosser were disclosed at this court-martial, after argument as to their admissibility. This is not in conformity with the usual practice and I am looking into the matter further.

Doctors and Shared Telephone Lines

Miss MARGARET HERBISON asked the Assistant Postmaster-General if he would ensure that no medical consultant had to share his telephone with another subscriber.—Mr. L. D. GAMMANS replied: Medical consultants are always given exclusive service at their surgeries or consulting-rooms, but all doctors are liable to share the telephone lines to their private houses if they do not practise there. This arrangement has applied since January, 1948, to all new and removing residential subscribers.

Miss HERBISON: Is the Minister not aware that it may lead to serious difficulties if the other subscriber should be using the telephone at the time when the hospital wishes to get into touch with the consultant about some important case? Is it not also of the greatest importance that a consultant's discussions with anyone in the hospital should be absolutely private? Mr. GAMMANS: When doctors are asked to share telephone lines we try to find them a suitable person with whom to share—such as a lock-up shop—so that during the hours at which he is presumably not at the hospital the doctor has virtually an exclusive service.

Mr. ARTHUR WOODBURN: Is the Minister aware that in Scotland it is the usual practice for a practitioner to have no private life at all. He is at the disposal of his patients night and day and it is quite inappropriate that people should have to talk to a doctor about their private affairs when somebody may be listening in? Mr. GAMMANS: Yes, but if a doctor uses his house as a consulting-room he is given an exclusive service. Mr. WOODBURN: Is the Minister not aware that even though doctors have consulting-rooms they still allow their house to be used in addition for the ordinary purposes of practice?

Influenza Vaccine

Mr. N. N. DODDS asked the Minister of Health if he could make a statement on progress made in the experiments with an influenza vaccine.—Mr. IAIN MACLEOD replied: The results of the trial of a new influenza vaccine carried out last winter have now been given preliminary study by a committee of the Medical Research Council. Over 12,000 people took part in the trial. Influenza was diagnosed in 3% of the group given the new vaccine and in 4·9% of the group given an older type of vaccine. 6340 volunteers received the new trial vaccine of the virus A type, and 192 had influenza. 6370 received an older type and 309 had influenza. These results are considered to be sufficiently encouraging to justify further research on the vaccine with a view to improving it.

Medicine and the Law

Swab left in Body

AT a recent fatal accident inquiry in Glasgow [1] undertaken by the sheriff (the Scottish equivalent of a coroner's inquisition in England) there was evidence that a large abdominal swab had been found in the body of the deceased. A major abdominal operation had been performed on a patient aged 66. Between four and eight large swabs and between thirty and forty smaller ones had been used. In answer to the sheriff the operating surgeon said that the senior surgeon had to accept considerable responsibility for the general organisation of work in the theatre and had to be sure that the nursing staff were efficient and that they understood their duties; subject to that, the actual counting of swabs was left to the nurses. Dr. Andrew Allison, emeritus professor of forensic medicine at St. Mungo's College, Glasgow, stated that the operation had been properly performed. Asked by the depute-fiscal whether the patient might have died even though no swab had been left in the body, the witness replied that the swab introduced irritation; the cause of death was a culmination of conditions—peritonitis, pneumonia, frequent vomiting, and a fatty heart.

During the inquiry it was stated that the operation began in the morning before lunch-time and went on till after lunch and there was a change-over of nurses while it was in progress. Care would be taken in future not to have a change-over during a major operation. A further precaution to be taken in future was the sewing of tapes on to the swabs in order to assist the surgeon in detecting the presence of swabs in the body. The jury returned a formal verdict of accidental death. The sheriff, in addressing them, pointed out that the medical and nursing staff had been extremely frank about the swab; the unfortunate accident appeared to be due to "a failure in the human element." The operation, said the sheriff, might have been successful, or it might not; the patient's chances, even without the swab, were not too good.

The case, with its account of safeguards introduced after the fatality, speaks for itself. The fact that the deceased had a limited prospect of surviving the operation, so often emphasised when accidents of this kind occur, might be an important consideration in reducing the damages in an action for negligence; it is entirely irrelevant to the question whether all possible care was taken in a matter of hospital routine.

1. *Scotsman*, July 17.

In England Now

A Running Commentary by Peripatetic Correspondents

AT our hospital the Death Meeting takes place once every two months. The medical staff, fortified by strong coffee and chocolate biscuits, meet round a table to review the deaths in the hospital during this period. Some selection takes place beforehand, for even in a small hospital the number of deaths is usually too great to discuss usefully in one evening.

Such a meeting is a good opportunity for the interchange of knowledge and views between the specialist branches of medicine. The realisation of failure may be lightened by the discovery that others have had similar experiences; but the criticism of wiser colleagues, albeit kindly and veiled in anecdotes, is a spur to better performance. The pathologist, benignly looking over his spectacles, reveals the ultimate facts, for necropsies are encouraged and the meeting is often a refresher course in morbid anatomy. It is surprising how often gross lesions, unrelated to the cause of death, are not suspected during life.

Matter for thought is sometimes provided by the heroic efforts of surgeon and anæsthetist to save a chronic invalid with some acute condition. For instance, a bedridden patient with gross hypertension and mental changes, uncoöperative and irresponsible, has his strangulated hernia operated upon, only to die a few days later. Do we sometimes try to defeat Nature's efforts to end a useless life? I remember one day telling my mother of an old lady of 84 who had survived operation for a perforated duodenal ulcer. "James," she said, "if you ever let anyone save me from my natural end at 84, I shall never forgive you." And the old lady with the ulcer lived on miserably for months, alone in one room, perpetually complaining of her indigestion. Perhaps she should have had partial gastrectomy instead of simple closure of the perforation.

* * *

One electron looks very like another to me and cathode-ray tubes are just something my wealthier friends use to decorate their living-rooms. Consequently a visit to the eighth annual exhibition of electronic devices of the North-West Branch of the Institute of Electronics was something of a revelation. There were, of course, the medical exhibits—the heart-lung machine from Hammersmith, an electron microscope, and a flying-spot microscope—but there were a lot of other exhibits at whose use I could barely guess. I would wander by a bench, and there on a larger or smaller screen a busy spot of brilliant light would execute its fantastic *pas seul*, tracing incredible patterns indicating almost everything from the magnetic field in the region to an analysis of any convenient spectrum.

Like all young sciences, electronics has developed its own jargon, and it was not uncommon to overhear a conversation between an exhibitor and some earnest inquirer, often a schoolboy, in which at least half the words were completely new to me. Ashamed of displaying my ignorance, I never did find out what an alignment wobbulator is, or what a photo-slubber does. Demonstrations of colour television reinforced my excuse for not buying an ordinary set "because colour will be here soon," and the ultrasonic drilling equipment looked just the job for boring holes in glass slides.

Despite all these marvels the thing I found most fascinating was a real, live, human, scientific glass-blower in a corner, nonchalantly blowing the most delicate and convoluted apparatus with less difficulty than I have to make a Pasteur pipette.

* * *

SURGERY: 1933 STYLE

Sir Reginald Quicke-Slyce left the operating-table, his work for the morning ended. While his registrar completed the closure of the abdomen he spoke a few brief words on the last case to the gallery filled with admirers who had come from all parts of the world to see the master at work. Sir Reginald was renowned for his courtesy and, after bidding his audience good morning, he thanked his theatre sister and then turned to his anæsthetist. "I must thank also my young colleague, Dr. Smother, for his skill in administering the anæsthetic to my patient. After all," he added waggishly, turning again to the audience, "we surgeons could not get very far without some sort of anæsthesia for our patients."

SURGERY: 1963 STYLE

Sir George Gagan-Smother moved away from the operating-table and faced the concourse of celebrated doctors who, for the past few hours, had remained spellbound by the quickness and manipulative dexterity of the mæstro. He was renowned for his courtesy and, after thanking his audience for the honour they had done him in attending his operating-session, he turned to his theatre sister and thanked her also. "And now," he said, addressing himself to the young man at the operating-table who had just completed his task, "I must thank you also, Dr. Chop, for the skill and experience which you have demonstrated in your handling of my patient. After all," he added waggishly, turning again to the gallery, "I suppose there would not really be much point in our administering an anæsthetic if we did not have a surgeon to perform some sort of operation on our patients."

* * *

The sun was shining on the land,
  Shining with all his might;
He did his very best to make
  The N.H.S. look bright—
And this was odd because there was
  No Guillebaud in sight.

With Whitley wet as wet could be,
  Finance as dry as dry,
No hospitals were being built,
  Though plans were piling high,
You could not see Macleod because
  Macleod was in the sky.

A Matron and a Secretary
  Were walking close at hand;
They wept like anything to see
  The waiting-lists expand.
"If these were only cleared away"
  They said, "it would be grand."

"If seven men had seven beds
  On loan for half a year
Do you suppose," the Matron said,
  "That they could get it clear?"
"I doubt it" said the Secretary,
  "But I'll Minute it, my dear."

A Superintendent looked at her,
  But never a word he said;
The Superintendent winked his eye
  And shook his learned head,
Meaning to say he'd not disclose
  Who had a vacant bed.

But four old patients hurried up
  With notes from their G.P.,
Their teeth were brushed, their bodies washed
  Consent forms signed for three—
And this was odd because in truth
  No single bed was free.

* * *

Scientific papers are increasingly beset with references extending, if one is good at that sort of thing, back to the Egyptian papyri. Have any of us given a thought to the predicament of our colleagues a couple of centuries hence? Many of their most important discoveries will have been first reported in the science fiction of today. The article on Health Rays and Healing Beams in this journal in 5391 will probably start:

"The earliest mention of these basic principles of Nature are found in articles by Smith (*Astounding Wonder Stories*, 1949, **5**, 301), Jones (*Galactic Marvels*, 1950, **3**, 71), Brown (*Super Science Tales*, 1951, **9**, 33), and Blank (*Space Adventure*, 1952, **4**, 27).

The author's task will be more entertaining, however, than that of those who seek out historical material in the Hungarian literature for 1880.

Letters to the Editor

OBESITY

SIR,—As another of your correspondents, apropos of a very different subject, has pointed out, the suppression of inconvenient evidence is an old trick in our profession. The subterfuge may be due to love of a beautiful hypothesis, but often enough it is due to a subconscious desire to simplify a confusing subject. It is not many years ago that the senior physician of a famous hospital was distinctly heard to remark, sotto voce, "medicine is getting so confusing nowadays, what with insulin and things." It is a sentiment with which almost everybody who qualified more than a quarter of a century ago is likely to sympathise.

Not long ago, Dr. Rynearson, an authority quoted in your annotation on obesity (July 18), ably reduced the whole problem to simple arithmetic. If a patient is fat, it is because he eats too much, and if he is too thin it is because he eats too little: this was the burthen of his song. "When a patient says to me, 'Doctor, I have the appetite of a bird,' I say 'Yes, madam, of an eagle.'" This wisecrack produced loud and prolonged applause from a large audience at the Royal Society of Medicine almost every member of which was overjoyed to be able to sail at last into the waters of security piloted by so eminent a physician. But ignoring difficulties is a poor way of solving them.

Of course, fat must come from food. Even the most vegetative patient cannot abstract it from the circumambient air as the leguminoseæ abstract nitrogen. But it is no use to deny that some people become fat more easily than others and, when dieted, lose weight more slowly. The fact that there is no satisfactory explanation at present does not invalidate the truth of the observation. I have seen two sisters, leading almost identical lives (and both with normal metabolisms) one of whom ate enormously and was very thin, while the other strove ever unsuccessfully by strenuous dieting to control her waist-line. It was the thin one who was lazy, too. A relation of mine has the most voracious appetite of any woman I have ever been forced to feed. She has remained always in excellent health, but looks like a patient with anorexia nervosa.

Insufficient attention has been given to the anatomy of the adipose tissue. Is it possible that some people have more of it than others? You can't store fat if you have nowhere to store it. This is presumably the explanation of some of the lipodystrophies. Another relation of mine (not related to the lady previously mentioned) was fat on one side of her body and thin on the other. Unfortunately there was no necropsy. Dr. Rynearson cannot have been right about both sides of her.

Too much has been said about animal experiments in which damage to the hypothalamus results in a voracious appetite. These observations are almost universally accepted as the explanation of hypothalamic obesity in human beings. But clinical observations suggest that the corpulence which so often follows hypothalamic damage by infection or trauma in *man* is not necessarily associated with bulimia. One patient of mine lives quite contentedly (even when under close observation) on a diet of 800–1000 calories and does not complain of hunger. What hurts him is the low intake of fluid I have enjoined. Although he has also a low intake of salt, he is perpetually thirsty.

This brings up the question of water-retention. No-one has succeeded in proving experimentally that corpulent people are waterlogged. Most people who have failed thus have decided to drop the whole subject, which they have come to regard as faintly indecent. They have stopped prodding the shins of their fat patients. If they were to do so they would find that many of them are œdematous, and this would force them to think again and leave behind them the comfortable security of simple arithmetic.

Lastly, Sir, Pennington's idea of cutting out the carbohydrate but allowing plenty of protein and fat works excellently even if ketosis is not produced, and allows of a higher calorie intake than a proportionate reduction of protein, fat, and carbohydrate. I do not know why. The diet need not be monotonous. Many patients come to prefer it. If you do not believe me, I will present you with a copy of Mrs. Beaton.

London, W.1. RAYMOND GREENE.

SIR,—In your annotation (July 18) you say that Pennington [1] regards obesity as a compensatory hypertrophy of the adipose tissues and claims that a ketogenic diet, consisting of fat and protein to the exclusion of carbohydrate, leads to a rapid loss of weight. One does not dispute the validity of a loss of weight on a ketogenic diet, but only the interpretation of the mechanism. In 1944 in a study [2] of the loss of weight of obese patients on submaintenance diets, I found that the greater weight loss of obese subjects on high-fat diets, as compared with that on high-carbohydrate diets, of equal calorific value, was due to the higher salt content of the high-carbohydrate diet, leading to retention of water and salt. When the salt content of the high-carbohydrate diet was reduced to that of the high-fat diet, the loss of weight was the same on both diets. This water-salt retention by obese patients is of practical importance in treatment by low-caloric diets. It is often found that after putting the patient on such a diet there is very little loss of weight at first, owing to water retention, and the patient is disappointed and loses faith in the treatment. If a low-salt diet is given from the beginning the weight loss begins at once, to the satisfaction of both patient and practitioner.

North Middlesex Hospital, London, N.18. A. B. ANDERSON.

ISONIAZID-RESISTANT STRAINS OF M. TUBERCULOSIS

SIR,—In their paper last week Professor Knox and his colleagues refer to a preliminary communication [3] from these laboratories in which some growth characteristics of isoniazid-resistant variants of *Mycobacterium tuberculosis* were described. One of the phenomena recorded was the ability of the izoniazid-resistant variant of H37Rv to grow in a synthetic medium which had been in contact with activated carbon for two days. No deduction was made from this experiment, however, nor was it claimed to have been shown, as Knox et al. state, "that isoniazid-resistant variants of *M. tuberculosis* are much more easily inhibited than sensitive strains by some substance which can be extracted from laboratory media with charcoal."

This obvious deduction, which Professor Knox and his colleagues have unconsciously attributed to us, may be correct. But other experiments which we have since carried out indicate that it may be an oversimplification. Thus, if in place of the carbon treatment, ash prepared from the carbon is added to the medium, growth of the H37Rv-resistant variant takes place. This ash is rich in iron, and we were thus led to examine the effect of adding ferric chloride in varying concentrations to the synthetic medium. It was found that with a concentration of 1 in 4000 of ferric chloride in the medium, growth of the resistant variant was as strong as that obtained by incorporation of 5% serum.

Another simple deduction could be made from these experiments: that the function of the activated carbon is to add iron salts to the medium, which promote the growth of the resistant variant. But this, too, is an

1. Pennington, A. W. *New Engl. J. Med.* 1953, **248**, 959.
2. Anderson, A. B. *Quart. J. Med.* 1944, **13**, 27.
3. Barry, V. C., Conalty, M. L., Gaffney, E. *Lancet*, 1953, **i**, 978.

unsafe deduction, for we have found that in the original experiments, sugar charcoal may be substituted for the activated carbon. This form of charcoal does not contain the quantity of iron salts necessary to promote growth. It is probable, therefore, that more than one effect is involved.

We hope to publish a full account of these experiments in the near future.

Laboratories of the Medical Research Council of Ireland, Trinity College, Dublin.

VINCENT C. BARRY
MICHAEL L. CONALTY
ETHNA GAFFNEY
FRANK WINDER.

MECONIUM ILEUS

SIR,—Your annotation last week shows a rather over-simplified approach to this condition, and one which, by virtually equating it with fibrocystic disease of the pancreas, makes the outlook pessimistic.

The clinical condition called meconium ileus probably has a number of different causes. It seems to vary clinically from a single meconium embolus, causing obstruction from a few hours or days after birth and often relieving itself, to the case with massive over-production of meconium and early perforation.

At this hospital we have found tryptic activity in 3 of the last 4 specimens of meconium from patients with the type of "ileus" you discuss. The suggestion, put forward by Farber and supported by Bodian, that the primary site of disease is the pancreas in many ways explains the condition less well than the explanation of a pancreatic lesion secondary to the intestinal obstruction.

It would be unfortunate if the view that cases of neonatal meconium obstruction are followed by a progressive and usually fatal disease in infancy were to discourage surgeons from early and energetic treatment of meconium ileus.

Department of Pathology, Children's Hospital, Sheffield.

JOHN L. EMERY.

WHAT IS ULCERATIVE COLITIS?

SIR,—Mr. Brooke in his article of June 20 has attempted to divide ulcerative colitis into three distinct entities according to the region affected by the disease. In doing this he has, I think, confused ætiology with therapy. As a practical convenience, especially for the surgeon faced with grave decisions during the management of the disease, Mr. Brooke's classification has much to recommend it. Prognosis is better defined, and the form of treatment easier to choose. But he has made no case for considering proctosigmoiditis, ulcerative colitis, and ileocolitis separate pathological entities.

Mr. Goligher has already pointed out (July 4) that it is impossible to make any distinction between proctosigmoiditis and ulcerative colitis involving other parts of the bowel. As a physician, who naturally sees more of the milder cases than a surgeon, I must support Mr. Goligher's contention that the endoscopic appearances are similar and the prognosis different only in degree. Many patients with ulcerative colitis involving only the rectum and sigmoid later develop generalised disease. Most commonly milder cases of ulcerative colitis are localised to the rectosigmoid, and the prognosis is relatively good. Other cases of ulcerative colitis, with the same granular non-ulcerative changes involving the whole bowel, may have few symptoms also; but the ultimate prognosis is worse than when the disease is localised. I have for two years observed three cases of ulcerative colitis localised to the transverse colon; symptoms have been intermittent and not serious. It is possible that it is the extent rather than the localisation of the disease in the colon which determines the prognosis.

I must also challenge Mr. Brooke's conception of ulcerative colitis as the degenerative end-result of a variety of pathological processes. Dr. Rice-Oxley (July 4) has already advanced several cogent reasons against this conception. It is a commonplace that endoscopic examination of early and mild cases of ulcerative colitis shows completely different changes from the advanced ulcerated condition of the colon seen in operation specimens. In no sense could these early endoscopic appearances be construed as degenerative; the mucosa is hyperæmic and swollen, the appearance wet and granular. Ulceration, as Mr. Goligher has pointed out, is not common in these mild cases. Histologically too, the early changes of ulcerative colitis are inflammatory rather than degenerative.

If one is searching for a conception of the pathology of ulcerative colitis, one must take into account its early inflammatory patchy distribution, its tendency to spontaneous exacerbations, remissions, and cure, and its predilection for youth, for certain races, and for certain types of personality. In my opinion there is a very close resemblance in all these respects to eczema of the skin.[1] It would be strange if eczematisation was confined to only the external surface of the body, although the variety of trauma to which the skin is subjected would explain its commonness in that site. The vulnerability of the colon would account for the severity of secondary infection and the dangerous complications of eczematisation as it affects the colon.

Bristol. J. NAISH.

SIR,—I have been interested in the correspondence about the distinction made by Mr. Brooke between ulcerative colitis and proctitis. The proctitis which Mr. Brooke describes deserves recognition, as do other forms of colitis, such as ulcerative colitis in its varying degrees of severity, regional colitis, relapsing colitis, chronic colitis, and non-specific ulcer of the rectum. Since the course and management in each form is different, a working classification is useful; but surely the ætiology of all forms is fundamentally the same.

No disease gives us a more disturbing example of how a viscus, and even a life, can be swiftly destroyed by an unhappy mental environment. All who have had experience of this condition will be familiar with these tragedies, occurring as they usually do, at an age when life should be full of promise. Almost invariably the significant situation becomes clear if a sympathetic and patient investigation is undertaken. Why one colon blushes throughout its whole extent and another only in part, why the mucosa of one colon may be so devitalised that it is digested and devastating secondary infection ensues, while the mucosa of another colon tends to heal, may for the present be legitimately regarded as an individual variation in the same pathological process.

What is important in this essentially modern disease is that the patient should receive help at the very onset of symptoms when the changes in the bowel are still reversible. The general practitioner, with, if necessary, the coöperation of close friends or relatives of the patient, is uniquely placed to support and advise the patient in facing and resolving the problem. I have seen a number of patients suffering from this disease whose life situations have been favourably modified in this way and whose colons have thus been healed. What is required perhaps is more practical psychiatry in the home, rather than specialised psychiatry in the hospital. The treatment of the specific problems of these patients may be more difficult and time-consuming than removing their colons, but who can say that this approach is not worth while.

This condition is one of the most suitable for intensive study by physicians and research-workers, in an attempt to establish the physiological connection between the hypothalamus, the endocrine glands, and the colon;

1. Naish, J. *Bristol med. chir. J.* 1952, 69, 5.

and a successful issue may well bring colitis, as Dr. Rice-Oxley prophesies, once more under the ægis of the physician. Meanwhile, when the changes in the colon are deemed irreversible or the patient's life is in danger, the best chance of restoring health is by radical surgery, undertaken as soon as possible. The thoughtfulness of surgeons in special centres, who have perfected surgical technique and improved the appliances for the patient, has made ileostomy and excision of the colon an operation which offers the patient a safe, comfortable, and unrestricted life.

Ilford. D. LANG STEVENSON.

RELIEF OF MENTAL HOSPITALS

SIR,—Dr. Atkin (July 4) seems to overlook the fact that a mental hospital is, to all intents and purposes, an institute for detention; and no separate units within its walls would alter that feature. Moreover, the time when every mental hospital will have such units is in the remote future.

The need for relief is very acute in all parts of the country; and we have to rely on buildings already standing and staffed. At several general hospitals I have found rooms unused. These rooms could be converted into units of the sort I have proposed; and, like very many mental hospitals, they could work without having the full staffing described by Dr. Atkin as indispensable. Surely, too, the overcrowding of mental hospitals is to a great extent due to admission of patients who should be in a general hospital.

I should have understood Dr. Atkin's reluctance better if he had been writing from a general hospital rather than a mental hospital. We are, however, in full agreement on one point: like him, I believe that my proposal to set aside general-hospital beds for mental patients is unlikely to get much immediate support from other specialists. But I also believe that the time has come when it should be recognised that psychiatry is no less than medicine plus the art of understanding the mind. Medicine has reached a point where it can get little further without the aid of its crude but powerful and rapidly growing younger brother.

Dingleton Mental Hospital, Melrose. J. W. MULLNER.

ANÆSTHESIA AND CLINICAL INVESTIGATIONS

SIR,—With the principle stated in your leading article last week few would disagree. You say "that the only factor limiting the use of anæsthesia for this [pneumoencephalography] and many other investigations that entail distress should be the number of trained anæsthetists."

However, it is one thing to define a limiting factor, and quite another to remedy it. Over a decade ago, I found that the duties of anæsthetist in a large teaching hospital could be accomplished by a mixture of guesswork and common sense. Since that time it has become obvious that sheer practice and experience, however extensive, is not adequate without proper training.

To my mind, the most serious question posed by the consideration of anæsthetics and clinical investigation is that of training. Trained anæsthetists are not unduly numerous; and senior anæsthetists, who alone can pass on their special skill, are even less numerous. One has seen the stiffening of the standards for anæsthetic diplomas—and rightly, for the responsibility carried by the anæsthetist has increased very greatly. Experience has shown that even after the potential anæsthetist has been allowed time to become a reasonably experienced clinician, at least two years of uninterrupted training and supervised work, solely in anæsthetics, is necessary before anæsthetics for clinical investigations should be tackled.

Whereas at an operation, an experienced surgeon is present (at least as counsel and companion in crisis), large parts of a clinical investigation may be entrusted to technicians. As a rule these technicians are well trained and qualified in their special task, but lack the broader background of clinical experience. The anæsthetic may be prolonged long after the removal, for example, of a lumbar-puncture needle. The anæsthetist may often find himself virtually alone to deal with dangers and difficulties, arising, not from the anæsthetic, but from the essential nature of the investigation. The better the anæsthetist, the more likely these are to occur; for good anæsthesia encourages thorough and methodical investigation, which takes a long time.

Investigation like this is greatly to the advantage of precise diagnosis, and anæsthesia is of real value, for the conscious patient simply cannot tolerate the ordeal of lengthy posturing. In addition, the anæsthetist may adjust the blood-pressure to assist the insertion of the needle in carotid or vertebral arteriography.

I, for one, would reject absolutely the idea that patients should go home after a long anæsthetic, whatever the agent. To persist in such a practice would, in my opinion, guarantee a collision with untoward circumstance—sooner or later. The first twenty-four hours after an anæsthetic belongs to the anæsthetist to follow up his case, and it should be claimed as a right. As there are rarely surgical considerations after such investigations, these cases offer particular scope for observation and clinical examination in the postanæsthetic phase.

Watford Maternity Hospital, Watford. J. NOEL JACKSON.

IDIOPATHIC HYPERCALCÆMIA IN INFANTS

SIR,—"Marasmus," so named by our predecessors but a mystery to them, is no longer considered to be a single disease, and (as you noted some months ago [1]) many of the different conditions included under this general term have now been separated off. As we turn the fine adjustment of the diagnostic microscope, it is most important to avoid confusion in our new and, we hope, more accurate terminology. Confusion at any stage, especially at the beginning, can easily hinder progress; meticulous care must therefore be taken over nomenclature. Ideally each new disease name should indicate the ætiology; when this is not yet possible it should be accurately descriptive, preferably in terms of function and structure; failing this it must be simply clinical.

Attention is now being directed to a group of disturbances affecting infants in which chronic hypercalcæmia is present, not associated with overt poisoning by vitamin D or with hyperparathyroidism. The nomenclature used in the description of these cases of hypercalcæmia will not be easy until more is known about them and especially about their ætiology; for the moment we can only label these syndromes descriptively. One type of syndrome manifesting hypercalcæmia has been labelled by observers in England and in Switzerland, as follows:

> Generalised retardation, with renal impairment, hypercalcæmia, and osteosclerosis of skull. (One patient, described by Butler.[2])
>
> Chronic hypercalcæmia with osteosclerosis, craniostenosis, and cortical nephrocalcinosis. (One patient, described by Fanconi.[3])

Subsequently, these English and Swiss patients were more fully reported under the title "Chronische Hypercalcämie, kombiniert mit Osteosklerose, Hyperazotämie, Minderwuchs und kongenitalen Missbildungen" by Fanconi et al.[4]

Another syndrome occurs, more common than the first, which is more benign and shows a less distinctive

1. *Lancet*, 1953, i, 78.
2. Butler, N. R. *Proc. R. Soc. Med.* 1951, **44**, 296.
3. Fanconi, G. *Schweiz. med. Wschr.* 1951, **81**, 908.
4. Fanconi, G., Girardet, P., Schlesinger, B., Butler, N., Black, J. *Helv. pædiat. Acta*, 1952, **7**, 314.

clinical picture (anorexia, vomiting, wasting, constipation, thirst, polyuria, and sometimes dehydration); for this syndrome the term "idiopathic hypercalcæmia in infants with failure to thrive" has been suggested as a temporary descriptive label [5] and accepted as convenient by Payne.[6]

The interesting single case-report published by Dr. Creery (July 4) under the title "idiopathic hypercalcæmia of infants" is the first example of "generalised retardation with renal impairment, hypercalcæmia and osteosclerosis" to be described in *The Lancet*. In this case the features do not match those which characterise "idiopathic hypercalcæmia with failure to thrive," and they are typical of the syndrome described by the Swiss and British workers. It is therefore unfortunate that Dr. Creery did not use one of the labels already applied by these workers. It is important to make this point in order to prevent confusion arising at this stage of clinical description when our understanding is limited, since it is so difficult to change wrong names when once they have been published and indexed.

There are certain clinical features which serve to distinguish the cases of simple idiopathic hypercalcæmia of infants from those with general retardation and osteopetrosis.

(1) The simple hypercalcæmias are transient and benign, there is no peculiarity of the facies, no distinctive bone changes, no cardiac bruit, and probably no hypertension. It is probably significant that an associated renal acidosis is occasionally found, perhaps in about 1 case in 5. The serum-calcium is raised from about 12 mg. to 18 mg. per 100 ml.; and the blood-urea is usually raised to about 70 mg. per 100 ml. As a rule recovery begins to take place in a few weeks; coincidentally the blood chemistry returns to normal and the infant resumes its natural gain in weight. Afterwards the intelligence is apparently normal.

(2) The cases with osteopetrosis have skeletal changes resembling Albers-Schönberg disease. The chemical changes in the blood are similar to those of simple hypercalcæmia except that there may be a rise in the blood-cholesterol; apart from this, there is at present no other chemical method of discrimination. An important clinical sign is the presence of an impressive systolic murmur. There is no evidence that this is due to congenital heart-disease, as Dr. Creery (following Schlesinger et al.[4] postulates in his case; the systolic murmur is probably due to hypertension. Both mental and physical progress is much retarded in these cases and, although some general improvement takes place, the mental state usually remains poor in our experience. It seems too that the facial appearance may be characteristic: the mouth is very wide, the upper lid is often thick and deeply bowed, the mandible recedes, the ears are set low on the head, and the child looks ill-tempered and unhappy.

Although we believe that these two clinical pictures may be different syndromes, the reverse is possible. This is a problem to be solved by the study of many more cases and, in order to do this, future clinical reports should, as far as possible, give the following data:

(1) Clinical photographs demonstrating the facies both early and late in the progress of the disease.
(2) Radiographs showing the skeletal changes at different stages.
(3) Radiographs of the kidneys at different stages.
(4) Blood-pressure readings, preferably made by careful adherence to a well-recognised technique, such as the flush method.
(5) A follow-up report and estimate of the mental age.

We would be grateful to hear of any such cases which the clinician concerned does not himself wish to publish.

St. Mary's Hospital Medical School, London, W.2. REGINALD LIGHTWOOD
THOMAS STAPLETON.

5. Lightwood, R. *Proc. R. Soc. Med.* 1952, **45**, 401; *Arch. Dis. Childh.* 1952, **27**, 302; *Arch. franc. Pediat.* 1953, **10**, 190.
6. Payne, W. W. *Arch. Dis. Childh.* 1952, **27**, 302.

N.H.S. PRESCRIPTIONS

SIR,—I have just received the Ministry of Health circular on Proprietary Preparations.[1] I wonder if I am alone in thinking that this merely scratches at the surface of the prescribing problem.

I would suggest that all drugs can be classified with a large measure of agreement into two categories:

1. Those that have a proved therapeutic effect in countering disease processes (e.g., antibiotics) or controlling major symptoms (e.g., hypnotics and antispasmodics).
2. Those that have no such proved effect and are used largely as vehicles for suggestion (e.g., tonics).

It is arguable that only drugs of the first category are irreplaceable therapeutic agents, and if free prescription was limited to them it would make a very big saving in the drug bill. This need not limit the doctor's prescribing since the other drugs could be available at the patient's expense; and in so far as they are unessential it does not seem unreasonable that they should be paid for.

However unpalatable it may be to vote-seeking politicians, the scope of the health service must clearly be limited by the funds available. At present a high proportion of these funds is being ineffectively applied to provide unessential drugs. No action on the part of prescribing doctors will materially reduce this waste unless it is supported by an official declaration that money available is for the free provision only of drugs that have an agreed therapeutic value. A less narrow field of free prescription must divert funds from other more effective measures in the fight against disease.

Marlborough College, Wiltshire. T. A. A. HUNTER.

VENOUS LIGATION AND POSTPHLEBITIC SEQUELÆ

SIR,—It would be unfortunate if the unqualified statement in the last sentence of the summary of the paper by Professor Boyd and his colleagues (July 18) should be too unreservedly accepted, and if it should discourage further cautious controlled investigation of this method of treatment.

Admittedly, the objective findings, as shown in the figures quoted for venous-pressure measurements, do appear to offer convincing proof that the operation fails to improve the venous return. Many workers, however, have found that the clinical results of the operation are very much more favourable than has been Professor Boyd's experience. Moore [2] recently reported 23 such cases, followed for from nine months to three years, and there was complete relief of symptoms in 18 of them, and in no case was there deterioration or undesirable side-effects.

The argument of Professor Boyd and his colleagues against major venous ligation in the treatment of chronic gravitational ulcer is greatly weakened by three facts: by their inclusion of 12 cases which had no ulceration; by the variety of levels at which the vein was tied; and by the large proportion of cases (the actual number is unspecified) in which the operation was combined with local excision and grafting of the ulcer. Few will agree that "femoral ligations are without doubt the least unsatisfactory": indeed, most workers who have tried both have reached the opposite conclusion. The poor long-term results of any type of grafting operation in these legs have been a disappointment to many surgeons; and vein ligation cannot be fairly assessed if it is combined with an operation which has such notoriously poor late results.

The authors state—alarmingly—that 6 out of 15 patients whose popliteal veins were tied became much

1. See *Lancet*, July 25, 1953, p. 194.
2. Moore, H. D. *Ibid*, 1953, **1**, 23.

worse. But they do not give the details which would enable the selection of these cases for operation to be criticised.

I have myself done 10 of these operations, ligating the popliteal vein at the upper limit of the popliteal space, where it is usually a single trunk; not one of these cases has shown any deterioration. Moore performed 23 popliteal ligations, with ill effects in none. The small number of my cases reflects the very rigid criteria used in the selection of patients for operation—these are the only 10 legs, in a series of over 160 cases of chronic ulcer, in which I have been satisfied on clinical and radiological grounds that the operation could be expected to do good. Of the 10 legs operated on, 2 show little change; the remainder are all greatly improved, and 4 of them dramatically so. These operations were all done as an isolated procedure, uncombined with any local treatment or ligation of other veins; and were only done when all other measures, including the adequate surgical treatment of superficial varicose veins, had failed to prevent recurrent ulceration.

It may well be that time will prove Professor Boyd and his colleagues to be right. But, narrowing the discussion to the consideration of ligation of the popliteal vein alone, performed only in cases of recurrent ulceration which have not been cured by adequate attention to superficial varices, adequate support of the limb, and the education of the patient in limb hygiene, I consider that the evidence in this paper does not justify the dogmatic statement that ligation of a major vein hinders the venous return from the lower limb; and that there is ample justification for surgeons to continue—albeit with the greatest of discrimination—the use of this method in suitable cases.

Queen Mary's Hospital, Roehampton, London, S.W.15. ALLENSON G. RUTTER.

LUPUS ERYTHEMATOSUS TREATED WITH CHLOROQUINE

SIR,—I was interested to read Dr. J. C. Shee's letter in your last issue. Last November I started treating lupus erythematosus with chloroquine sulphate, and I shall be publishing an article about a number of such cases as soon as the normal period of summer (if this exists) is over.

Radcliffe Infirmary, Oxford. H. J. LEWIS.

CÆSAREAN SECTION

SIR,—I read with interest your annotation of July 4.

May I enter a plea for the careful use of a low vertical incision in cæsarean-section operations. This is supported by a personal series of more than a hundred consecutive cases at the Victoria Hospital, Deal, with no maternal deaths or complications.

I am sure that adhesions can be prevented by careful suture and inturning of uterine peritoneum. There is one patient in the series who had five cæsarean sections and was still free from adhesions when the last was done. All the children are alive, and she is free from pelvic trouble many years later.

The great advantage, to my mind, is that the technique is suitable to every complication of labour, and that blood-loss can be reduced to a minimum by any intelligent assistant who maintains a strangling grip round the uterine arteries till the placenta is removed and the incision closed. It is difficult, if not impossible, to apply this blood-saving technique to the lower-segment operation; and although we make good the loss with transfusions these are dangerous things to give women of childbearing age in view of the Rh factors.

I have never used anything except no. 4 catgut for uterine suture, and am completely satisfied with the subsequent result. The uterine scar is not detectable at second operations, and several cases where the obstruction to birth has not been pelvic have had subsequent normal labours. It is perhaps germane to the argument that the bulk of the series cited above are failed forceps cases, some in very poor physical condition and nearly all in the pre-antibiotic era. This leads one to believe that safety in surgery may be found in more careful use of classical operations as well as in devising new modifications which must at first be experimental. I believe it was Doyen who said that the successful surgeon arose from a mountain of corpses. Another comment, in your own journal, was that the surgeon is judged by the calendar and not by the clock.

These memorable sayings plead for extreme personal care in technique, and the choice wherever possible of a routine operation in which the individual surgeon has learned all the pitfalls.

Deal. JAMES S. HALL.

TUBERCULIN MONITORING OF INDUSTRY

SIR,—The epidemiological unit in tuberculosis is the group in contact (i.e., under conditions suitable for the transfer of infection should an infector be present), which I have termed a congregation.[1] One, but only one, such unit is the family. Another is the work contact group, which has received less attention than it deserves. The existing mass X-ray units can only examine some 7% of the population per annum.[2] The amount of time devoted to the factory worker has perforce become less recently, as the sessions for the general public with their higher yield of active cases are increased.

I should like to propose for trial an epidemiological remedy for the neglect of tuberculosis in industry, as a stopgap until resources improve. Briefly, I suggest a combination of serial tuberculin testing and mass radiography, which we may term the tuberculin monitoring of industry. If the risks of a group are indicated by risks of individuals "sampled" from that group, it would seem that the serial tuberculin testing of young uninfected entrants into the larger workshops or offices would offer a (not infallible) guide to where infection is actually occurring. Such a continuous procedure of mass supervision, once in operation, would enable us to pinpoint the workplaces in which a source of infection was or was not probably present. The persistently rapid conversion of new negative entrants to a particular workshop would indicate the need for a mobile mass X-ray unit to visit the place. Such a unit would have to be highly mobile. It would spend its time "chasing" sources of infection in industry, its programme being "indicated" for it by the tuberculin monitors. The unit would by the tuberculin supervision of a mere fraction of young people in industry be able to keep an over-all eye on where infection is occurring and take immediate steps to locate the source cases. Of course many such tuberculin-guided case-finding surveys would draw a blank, since young people can be infected at places other than at work. Nevertheless, where the number of fellow workers in the same room greatly exceeds the total of family and friends one would think that a source of infection, if existing, would be more likely to be found in the larger group at work. Radiographic case-finding by tuberculin monitoring of an initially negative fraction of people in industry should uncover a number of cases that might not be found by other means, and many would be partially safeguarded from exposure to unknown sources of infection by the tuberculin testing of a few.

The scheme suggested differs from the tuberculin matriculation of Gedde-Dahl[3]—i.e., continuous tuberculin testing of the *whole* population—in that only small *fractions* of large groups in contact at work would be tested. "Gedde-Dahl recognises that tuberculin

1. Nash, F. A. *Tubercle*, 1953, **34**, 105.
2. Harley Williams, J. *Bull. int. Un. Tuberc.* 1952, **23**, 512.
3. Gedde-Dahl, T. *Amer. J. Hyg.* 1952, **56**, 139.

matriculation is not feasible in urban communities with high infection-rates—there would be too many untraced infections." [4] The proportion of new infections that would be untraced would be highest where the infection had most probably been acquired casually and by people working only in small groups. Where a converter is working in a large group the chances of casual infection will be relatively less important than the chances of exposure at work. The radiography of workmates of converters in large workshops might therefore be expected quite often to show the source of the infection.

It might be difficult for a mass X-ray unit with many public commitments to test the practicality of such a scheme, and there is a need in most countries for at least one mass X-ray team free from " public service " commitments and able to devote itself to devising and trying better case-finding techniques.

Mass X-ray Service for South-west London, Grove Hospital, S.W.17. F. A. NASH.

ENDOCRINE TREATMENT OF MAMMARY CANCER

SIR,—I read with interest your annotation of July 11, which referred to treatment of cancer of the breast by hypophysectomy.

At my suggestion Dr. J. Le Beau, neurosurgeon at the Hôpitaux de Paris, did a hypophysectomy in a case of advanced cancer of the breast with metastases (stage 4). The operation was done on Nov. 29, 1951, and the result up to now has been good.[5] We did not know at that time that Olivecrona had done this operation for the same purpose.

It seems to us that this method is relatively safe provided that there are no cerebral metastases nor serious respiratory dysfunction. As to its efficacy, no conclusion is yet possible. Nevertheless, in this first case of ours, where the expectation of life would normally have been at most 3–5 months, the patient has already survived 20 months.

Paris, 7e. MARCEL PERRAULT.

CONTRACEPTIVE TECHNIQUE

SIR,—All contraceptive methods involving a mechanical barrier have disadvantages. Therefore, when responsible research evolves a new technique which does away with the objectionable barrier, and is supported by evidence from clinical trials in America [6] and elsewhere, then such a method would seem to warrant careful consideration.

Dr. Stopes (May 2 and 30) bases her criticism of the procedure not on its direct trial but on theory. She objects in principle to a vaginal applicator and does not mention the alternative—deep introduction of fingers and caps. She stresses her preference for a greasy spermicide base, when more modern non-greasy bases have been shown to be superior in cervical adherence, spermicide-releasing time, and dispersing power, while being free from unpleasant odour and linen-staining properties. She also emphasises the occurrence of direct intra-uterine ejaculation. This might occur if the external os were patent to an extent precluding its complete occlusion by a tenacious gel such as 'Preceptin.' Such cases are comparatively few and they can be excluded, on first examination, after direct inspection of the cervix.

Dr. Glaisher's objection (July 4) is based on but 2 cases, both of which were quite abnormal and of doubtful suitability for gel alone. It is not sufficient to deposit a standard dose of 5 ml. in the distorted posterior fornix, out of reach of a prolapsed cervix. It is essential to *see* that the cervix is well covered, if possible after teaching the patient to direct the applicator on to it, and if necessary by increasing the dosage to 10 ml. or more, so as to fill any deepened spaces. Again, a scarred and deformed cervix with perhaps a patent os and superadded infection can hardly be expected to show safe occlusion with gel alone.

Preceptin clearly cannot be safely advocated without clinical checking and at least such care and experience as is required for fitting a cervical cap. Undoubtedly the ease with which it can be " prescribed " without any examination is its greatest danger.

My own practice is to inspect the cervix at least three times: once to make sure it is in a healthy condition to take the gel; secondly just after injection to see how well the os is covered; and thirdly, on a different occasion, after the patient has injected herself and then travelled, walked about, and sat for at least two hours. One then finds that the degree of cervical occlusion varies considerably. It is good in most cases, with only minimal " leakage," but it is hardly adequate in some. The latter are immediately switched to another method, and only those with a well-covered os are allowed to go ahead with preceptin. Patients are also warned that the maximum safety-time is one and a half hours, after which coitus must be preceded by another injection. And they are told that if they wish to douche they must not do so until six hours afterwards.

The technique appears to be psychologically more acceptable to the sensitive. I do not claim that I have sufficiently evaluated this method; but I have used it successfully in selected private patients and in 17 psychiatrically disturbed patients for three to eleven months, with 1 failure, in the parenthood planning clinic of the Maudsley Hospital.

London, W.1. H. PETER TARNESBY.

MENTAL NURSING

SIR,—Those of us who are confronted daily with difficulties and problems which arise as a consequence of the shortage of nursing staff in mental hospitals welcome the helpful and constructive comments in your annotation last week. Your statement that the obvious thing to do for those recruits who are intellectually and educationally unfitted to deal with the curriculum for the State mental register would be to train them as State-enrolled assistant nurses is endorsed by a large number of hospital administrators. The fear that such a policy would be detrimental to recruitment of student mental nurses reminds us of the fear, expressed some ten years ago, that the establishment of the State-enrolled assistant-nurse grade would affect recruitment to the general student-nurse grade. Such a fear has proved to be unfounded, and where would we be without the services of the splendid assistant nurses whom we have in our hospitals today?

This grade is equally essential in our mental hospitals since recruitment to the student mental-nurse grade is so limited and since in future selection is to be more stringent. Furthermore, the gap between the trained mental nurse and the nursing assistant is too great and should, in order to give a balanced staff, be filled by assistant nurses.

The General Nursing Council could help considerably to foster such a grade if, for those pupil assistant nurses recruited to and trained in mental hospitals, a provision was made that they could be fully trained within that hospital. At the moment, approval for a pupil assistant-nurse training scheme for a mental hospital is conditional upon part of the training being undertaken in a children's hospital, and for female pupils, upon a further period being spent in a general hospital providing male bedside nursing. These requirements deter prospective pupils, often from the ranks of the mental hospitals' nursing assistants, and therefore limit the number of badly needed recruits.

Liverpool Regional Hospital Board. T. LLOYD HUGHES
Senior administrative medical officer.

4. *Lancet*, 1952, ii, 922.
5. Perrault, M., Le Beau, J., Klotz, B., Sicard, J., Clavel, B. *Thérapie*, 1952, **7**, 290.
6. Hunter, G. W., Darner, C. B., Gillam, J. S. *Ann. N.Y. Acad. Sci.* 1952, **54**, 825. Stromme, W. B., Rothnem, M. S. *Ibid*, p. 831. Finkelstein, R., Guttmacher, A., Goldberg, R. *Amer. J. Obstet. Gynec.* 1952, **63**, 664. Eastman, N. W., Selbels, R. E. *J. Amer. med. Ass.* 1949, **139**, 16. Hunter, G. W., Darner, C. B. *Jl.-Lancet*, 1952, **72**, 555.

Notes and News

COMMONWEALTH BURSARIES

THE Royal Society and the Nuffield Foundation are to initiate a Commonwealth bursaries scheme to provide facilities for investigators of proven worth to pursue research, learn techniques, or follow other forms of study overseas in the Commonwealth. The bursaries will aim not so much at obtaining the answer to a particular question as at improving the powers of the recipient to extend the bounds of knowledge.

For an experimental period of five years the Nuffield Foundation will provide £5000 a year for bursaries to United Kingdom scientists who wish to go to oversea parts of the Commonwealth and to scientists of one oversea part of the Commonwealth to go to another. Initially the Royal Society will also make a contribution of £2500 which will be available for movement in any direction within the Commonwealth, including to the United Kingdom. It is, however, hoped that funds may be obtained from other sources, particularly from overseas, so that more bursaries available for scientists of oversea countries of the Commonwealth who wish to study will be made in the United Kingdom.

Each bursary will provide for the cost of travel and maintenance normally for periods of two to twelve months. It will not aim at the provision of any salary as such but of sufficient maintenance to avoid frustration. The applicant must be sponsored by a recognised research authority and must have prior permission to work in the laboratory or other scientific institution chosen.

The membership of the committee set up to administer the scheme is as follows:

Chairman: Sir Edward Salisbury, SEC.R.S.

Nominated by Trustees of the Nuffield Foundation: Mr. Leslie Farrer-Brown, Sir John Stopford, F.R.C.P., F.R.S., Prof. A. R. Todd F.R.S.

Nominated by Council of the Royal Society: Prof. G. R. Cameron, F.R.C.P., F.R.S., Prof. H. S. W. Massey, F.R.S., Sir Eric Rideal, F.R.S.

Applications will be considered at six-monthly intervals beginning early in 1954. Further details may be had from the assistant secretary of the society, Burlington House, Piccadilly, London, W.1.

A SCHOOL OF MEDICAL PHOTOGRAPHY

THE training of medical photographers presents difficulties because photography as used in hospitals and medical schools ranges from the copying of documents to high-speed endoscopic photography. The techniques used include such diverse subjects as the different processes of colour photography, the use of infra-red and ultraviolet light, photomicrography (both still and ciné), the planning of exhibitions, and the production of teaching films, while the subject-matter extends through the whole field of medicine, including such ancillary subjects as embryology and spectrum analysis.

Till now training has been almost entirely by apprenticeship, with the disadvantage that a student can rarely get experience outside a limited section of his subject. The deficiencies of the present system have been emphasised by the results of the medical section of the final examination of the Institute of British Photographers which was set up five years ago.

In an effort to provide the necessary practical experience the heads of the photographic departments of eight London hospitals, postgraduate institutions, and medical schools have now established a combined training-school provisionally designated the London School of Medical Photography. Students, who must have had two years' general photographic training before admission, will have the opportunity of working and receiving instruction in all branches of medical photography. After two years they will be in a position to take the I.B.P. final examination and on passing will qualify for the register of medical photographers. In this way it is hoped to fulfil a demand for fully trained medical photographers.

MAIZE

ONE of the several gifts that the Old World received from the New, early in the 16th century, was maize. Today, in the whole world, over 138 million metric tons is grown each year, of which about 100 million tons is grown in the Americas. Of this huge total some 20% is eaten by man and the rest is used as animal feeding-stuff or as raw materials in industry. There are large populations in Mexico, Cuba, Venezuela, Rumania, Spain, Egypt, and South Africa whose principal food is maize and whose consumption of the cereal may be over 500 g. per head per day. The nutritive value of maize and maize diets is therefore a very practical problem.

Assisted by Dame Hariette Chick, the Nutrition Division of the Food and Agriculture Organisation (F.A.O.) have produced an excellent small monograph[1] on the subject, which should be widely read in all maize-eating countries. Maize has two great practical advantages over most other cereals: (1) it is hardy and thrives under widely different climatic conditions; and (2) it is a plant with a high yield—able, indeed, to produce more calories per acre than either wheat or rice. To offset these advantages there are deficiencies in the chemical content of the grain. All maizes are poor in tryptophan, the principle protein, zein, being almost devoid of this essential amino-acid. They are also deficient in nicotinic acid (niacin); and wherever maize is the stable food of the people pellagra has at some time become endemic. Rice can be equally poor in nicotinic acid yet not give rise to pellagra; for in some circumstances the tryptophan which rice contains can be converted into nicotinic acid in the body. Not only is maize almost devoid of tryptophan but there are strong reasons for believing that it contains an anti-vitamin antagonistic to nicotinic acid.

A great variety of maizes have been produced by plant geneticists, and in some of these the content of niacin and tryptophan has been raised. Systematic selection among these varieties may lead in time to the establishment of varieties of better nutritive value; though so far plant-breeders have been more successful in creating hardier and higher-yielding varieties than in changing the chemical composition of the grain. Supplementation of maize diets with other foods, to correct deficiencies, is the more practical immediate measure. Animal foods such as meat, eggs, fish, and milk are the most desirable additions; but they are expensive, and in some parts of the world almost unobtainable. Evidence is now accumulating that mixtures of other vegetable foods—notably legumes, beans, and nuts—can produce a well-balanced vegetable diet, suitable at least for adults.

The report is well documented and adds to the growing reputation of F.A.O. for collating and distributing knowledge vital to human welfare.

PORTRAITS AT THE COLLEGE OF PHYSICIANS

THE college has published a new catalogue of its collection of engraved portraits of medical and scientific men. The collection now numbers 4500 prints. Most of them are of British physicians, but some surgeons and medical men of other nations are included. The college also has 300 photographs of portraits of physicians and surgeons, and 700 photographs of 19th-century doctors which are available to biographers. Copies of the catalogue may be had from the college, Pall Mall East, S.W.1 (price £2).

AMENDMENT OF NATIONAL FORMULARY

THE first amendment[2] of the *National Formulary 1952*, now published, makes changes arising from the introduction, on Sept. 1 this year, of the *British Pharmacopœia 1953*. The amendment includes a table showing the labelling and identification colours for medical gas cylinders, in accordance with the revised British Standard code of practice. There are also a list of corrigenda and a Latin-English index of the formulary section headings.

University of Edinburgh

On Aug. 3, at 5 P.M., Prof. Shields Warren, of Harvard University, will deliver a lecture at the University New Buildings, Teviot Place, Edinburgh. He will speak on the Pathologic Consequences of Total Body Irradiation.

Scottish Conjoint Board

At recent examinations of the board of the Royal College of Physicians and Surgeons of Edinburgh and the Royal Faculty of Physicians and Surgeons of Glasgow the following were successful:

Rasul Bux Baluch, Cora Branker, Margaret P. Bruce, M. G. Cameron, Cyril Harris, Maureen E. Hillery, C. R. Johnson, Inderjit Khosla, Eleanor M. Kneale, Satinder Lal, Iain Grant Macpherson, J. G. Noble, Jagdish Singh Walia, Mary H. Wallace.

1. Maize and Maize Diets. A Nutritional Survey. F.A.O. Nutritional Studies, no. 9. Rome, 1953. H.M. Stationery Office. Pp. 94. 5s.
2. National Formulary, 1952: First Amendment 1953. London: British Medical Association and Pharmaceutical Press. 6d.

University of London

The title of professor emeritus of physics has been conferred on Prof. Gilbert Stead, D.SC., on his retirement from his chair at Guy's Hospital Medical School. Dr. G. D. Lumb has been appointed to the readershp in pathology at Westminster Medical School. The title of professor of experimental pathology has been conferred on Dr. A. A. Miles in respect of the post held by him at the Lister Institute of Preventive Medicine.

At recent examinations for academic postgraduate diplomas the following were successful:

D.P.H.—Isidore Ash, D. E. Boye-Johnson, Robert Bradley, J. H. Brodie, Jack Carlton, Gwen S. Clark, Claude Eid, A. J. Essex-Cater, R. S. Gibson, G. J. Glynn, L. P. Harington, I. K. Hay, Winifred M. Hiscock, G. B. Hopkins, Ibrahim Ahmed Hussein, Dorothy D. Jones, F. R. S. Kellett, A. J. I. Kelynack, J. H. Lewis, Khoon-Huat Lim, Bhaskar Mahadevan, G. P. Merson, Henry Mowschenson, F. G. Neild, Basil Nicholson, W. F. Ross, Sverre Sandmo, Monic Chand Sanyal, William Sheffield, J. H. Taylor, A. M. Thomson, D. E. Thompson, G. F. Willson, A. B. Wittek, C. H. Wood, David Yarom, Albert Zahra, Ahmed Ali Zaki.

D.T.M. & H.—E. B. Bright, Peter Jordan.

Royal College of Physicians of Edinburgh

At a meeting of the college held on July 21, with Dr. W. A. Alexander, the president, in the chair, the election of the following to the honorary fellowship was announced:

Prof. C. H. Best, F.R.S.; Sir Russell Brain, F.R.C.P.; Sir Macfarlane Burnet, F.R.S.; Sir Charles Hercus, F.R.A.C.P.; Sir Gordon Holmes, F.R.S.; Sir Robert Muir, F.R.S.; Sir John Parkinson, F.R.C.P.

The following were elected to the membership:

J. R. Bailey, W. A. Murray, M. A. Wafa, T. J. Danaraj, H. Foster, E. L. Davis, M. Macleod, R. S. Morton, M. Scott-Gray, G. J. V. Perera, D. E. P. Forbes, A. V. A. Vethanayagam, C. H. Gurd, H. P. Vaishnava, D. J. Gudex, Ata-Ul Haq, K. R. Tyler, R. W. H. Simmons, A. Pines, E. O. L. Hoskins, S. G. F. Wilson, S. I. Kuper, P. A. Rechnitzer, G. W. Allan, A. Nestadt, H. D. Jacobs, K. S. Husain, R. Kilpatrick.

Royal College of Obstetricians and Gynæcologists

At a meeting of the council held on July 25, Mr. Arthur Gemmell in the chair, the following officers were re-elected:

President, Mr. Gemmell; vice-presidents, Prof. Gilbert Strachan and Mr. A. J. McNair; hon. treasurer, Mr. A. C. H. Bell; hon. secretary, Mr. H. G. E. Arthure; hon. librarian, Mr. A. J. McNair; hon. curator of the museum, Mr. Aleck Bourne; hon. treasurer, Canadian regional council, Mr. W. R. Foote.

The following officers were elected:

Hon. treasurer, Australian regional council, Mr. J. N. Chesterman; hon. treasurer, New Zealand regional council, Mr. J. E. Giesen.

The Bernhard Baron scholarship was awarded to Mr. Stanley Way for research on the early diagnosis of cancer in women.

The following was admitted to the membership:

D. S. Burris.

The following were elected to the membership:

L. J. Abramowitz, Subrahmanyan Alankaram, W. J. R. Anderson, G. S. Andrew, Amiya Kumar Bose, J. C. Brace, E. R. Broadberry, T. J. Buckley, Samuel Burke, R. K. Burt, J. G. Cameron, Rory Shaun Casement, Po Wong Christina Chow, Maureen D. Connolly, R. L. Edwards, M. B. Flanagan, F. M. C. Forster, Kathleen M. Frith, M. C. G. Grant, P. B. Guastalla, R. H. J. Hamlin, J. W. S. Harris, C. A. Jones, R. Ll. Jones, I. R. Macdonald, Betty Mallace, G. A. Manly, D. N. Menzies, M. C. Michelow, John Nattrass, H. H. Neifeld, F. N. Neser, J. P. O'Dwyer, Dharma Rau Patnaik, Clara Phillips, B. G. Pickles, William Rotheram, J. S. Scott, J. M. Stewart, R. A. Struthers, Valerie M. Thompson, C. J. Thornberry, Harry Ulman, C. G. Wilson.

World Health Organisation

Dr. Brock Chisholm, the retiring director-general of W.H.O., handed over his duties to his successor, Dr. M. G. Candau, on July 20.

Empire Rheumatism Council

The council are holding a symposium on 'Butazolidin' (phenylbutazone) at 1, Wimpole Street, London, W.1, on Friday, Nov. 13. Tickets may be had from the general secretary of the council, Tavistock House (North), Tavistock Square, W.C.1.

International Society of Angiology

This society is holding its second congress in Lisbon from Sept. 18 to 20. The principal subjects chosen for discussion include Aneurysms (at a joint session with the International Society of Surgery) and Mitral Valvular Surgery. The secretary of the congress is Dr. J. Celestino Da Costa, R. Nova de St. Antonio 8-2°, Lisbon, Portugal.

Society of Apothecaries of London

The honorary mastery of midwifery has been awarded to Sir William Gilliatt, and the society's gold medal in therapeutics to Sir Charles Harington, F.R.S.

C. F. White, A. M. A. Moore, and Sir Lionel Whitby have been elected to seats on the court.

The following have been clothed with the Livery:

M. P. Hutchinson, A. W. Spence, J. G. Bulman.

The following have been admitted to the Freedom of the society:

A. C. Frazer, K. E. Harris, H. V. Schwalm, L. A. Lees, R. T. Hewitt, Alice M. C. Macpherson, G. G. Allan, H. C. Cameron, P. W. M. Copeman, William Gooddy, J. A. White, W. D. Park, C. G. A. Sadler, E. B. P. Madden, J. V. O'Sullivan, D. K. Mulvany, Frank Kellett, D. E. Wheeler, J. R. Hudson, Denis Browne, J. W. Barrett, Charles Seeley, A. J. C. Balfour, C. G. Teall, F. D. Hart.

P. J. Holmes Sellors Bound to T. Holmes Sellors for four years, and G. G. Muir to E. G. Muir.

The following diplomas have been awarded:

L.M.S.S.A.—T. P. Oliver, R. G. Orr, T. F. Stoyle, P. Jensen, S. T. Guest, J. Cottam, E. P. James, W. F. T. Davies, J. R. Croning, R. H. Morgan.

D.I.H.—C. P. Chivers, K. B. Roy, R. Whitelaw.

College of General Practitioners

The first annual general meeting of the college will take place on Saturday, Nov. 14, at 2 P.M., in the hall of the Society of Apothecaries, 14, Black Friars Lane, London, E.C.4.

British Medical Association

Is the Medical Curriculum Too Heavily Loaded? has been chosen as the subject of the association's essay competition for medical students for 1954. Essays must reach the secretary of the association, B.M.A. House, Tavistock Square, London, W.C.1, not later than Dec. 31, 1953.

Langdon-Brown Bequests

Lady Langdon-Brown, widow of Sir Walter Langdon-Brown, F.R.C.P., left £1000 to the Royal College of Physicians to form a Langdon-Brown Hospitality Bequest and £2500 to Corpus Christi College to form Walter Langdon-Brown scholarships. She also named the two colleges as residual legatees of her estate (£9000).

Foot Health Educational Bureau

This bureau, formerly directed by Mr. F. H. Bentley from 121, Ebury Street, London, S.W.1, has been incorporated in the Central Council for Health Education, Tavistock House, Tavistock Square, W.C.1.

The Proceedings of the Fourth International Congress of Mental Health, held in Mexico City in 1951, have now been issued under the editorship of Dr. Alfonso Millan. They are published in this country by H. K. Lewis & Co. Ltd., London, at 30*s*.

Rembrandts within Rembrandts.—Professor Plesch's monograph on the subordinate figures in Rembrandt's paintings (see *Lancet*, 1953, i, 956) has now been published in English (London: Simpkin Marshall. 1953. Pp. 120. 42*s*.).

Appointments

BENNETT, T. R., M.R.C.S., D.P.H.: asst. M.O., Surrey.

FRASER, H. A., M.B. Camb.: appointed factory doctor, Stowmarket, Suffolk.

South Western Regional Hospital Board:

BARKER, J. C., B.A., M.B. Camb.: registrar in diseases of the chest, Bristol clinical area.

BOULLE, J. R., M.B. Cape Town: surgical registrar, Taunton and Somerset Hospital.

RITCHIE, E. A., M.B. Lond., M.R.C.P.: registrar in psychiatry, Moorhaven Hospital, Ivybridge.

SIBTHORPE, ELSIE M., M.D. Lond., M.R.C.O.G.: senior registrar in obstetrics and gynæcology, Bristol clinical area.

Births, Marriages, and Deaths

BIRTHS

GRETTON-WATSON.—On July 16, at Chester, to Concetta, wife of Dr. B. G. Gretton-Watson—a daughter (Clare Lilian).

PARK.—On July 19, at 40, Wilbury Road, Hove, to Dr. Emily Park (née Smith), wife of Mr. Harold Park, F.R.C.S.— a daughter.

PURDIE.—On July 25, at the North Middlesex Hospital, London, N.18, to Erica Purdie (née Roberts), M.B., wife of Mr. Anthony W. Purdie, F.R.F.P.S., F.R.C.O.G.—a daughter.

DEATHS

VILVANDRÉ.—On July 26, at The Thatched Cottage, Redbourn, Herts, Dr. George Ernest Vilvandré.

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Academic and Educational

ROYAL COLLEGE OF PHYSICIANS OF LONDON

The next EXAMINATION for the MEMBERSHIP will commence on MONDAY, 28TH SEPTEMBER, 1953.

Prospective candidates are asked to note that entries accompanied by the certificates, testimonials and the examination fee of 15 guineas as required by the by-laws, must reach the College not later than first post on Monday, 31st August. Candidates must have been qualified for 18 months.

Candidates who propose to submit published work under the regulations are required to give 28 days notice, and should apply in writing to the Registrar, without delay, for detailed instructions as to the procedure they should follow. Completed entries for published work must also reach the College not later than first post on Monday, 31st August, 1953.

HAROLD BOLDERO, D.M., Registrar.

12, Pall Mall East, London, S.W.1.

ROYAL COLLEGE OF SURGEONS OF EDINBURGH

BASIC SCIENCE COURSE

2 COURSES IN THE BASIC SCIENCES (Anatomy, Physiology, Pathology, including Bacteriology) will be conducted by the Fellows of the College and others, under the ægis of the Edinburgh Post-Graduate Board for Medicine.

These courses, comprising lectures and demonstrations, will begin on 5TH OCTOBER, 1953, and 4TH JANUARY, 1954, and continue for 10 weeks. Fee 25 guineas.

Applications for enrolment, or further particulars regarding these Courses, should be addressed to : The Director of Post-Graduate Studies, Surgeons' Hall, Edinburgh, 8.

UNIVERSITY OF LONDON

GRANTS FOR RESEARCH

Applications are invited from members* of the University for grants from the Central Research Fund to assist specific projects of research and for the provision of special materials and apparatus. Grants are not made for normal maintenance.

Applications must next be received not later than 31st August, 1953. Forms of application and further particulars may be obtained from the Secretary to the Central Research Funds Committee, University of London, Senate House, London, W.C.1.

* Members of the University are defined by Statute as the Chancellor, the members for the time being of the Court and of the Senate respectively, the Professors and Readers and other Teachers of the University during their tenure of office, the graduates and the students.

CLINICAL POSTGRADUATE REFRESHER COURSE IN GENERAL AND ORTHOPÆDIC SURGERY

A Clinical Postgraduate Refresher Course in General and Orthopædic Surgery, consisting of 8 sessions (10 A.M.–12.30 P.M.), will be held at Fulham Hospital on consecutive SATURDAY mornings from 12TH SEPTEMBER to 31ST OCTOBER, 1953. A maximum of 10 students will be accepted.

Fee : 8 guineas (payable in advance).

Further particulars obtainable from the Secretary of the F.R.C.S. Course, Fulham Hospital, St. Dunstan's-road, London, W.6.

THE BERKELEY FELLOWSHIP

(Founded in memory of the late Sir G. H. A. COMYNS BERKELEY and his wife, ETHEL ROSE BERKELEY)

Applications from Graduates in medicine of the Middlesex Hospital Medical School are invited for the Berkeley Fellowship. Candidates should normally be under 35 years of age. The salary is £600 p.a., with certain extra allowances for travelling and research. The Fellowship is tenable normally for 1 year, but applications for renewal will be considered. Applications should reach the Dean of the Middlesex Hospital Medical School by 1st September, 1953. Broad outline of the programme of work or proposed itinerary, together with an estimate of cost, should be submitted with the application.

The Berkeley Fellowship was founded under the will of the late Sir G. H. A. Comyns Berkeley to provide research and travel facilities to a person elected jointly by the Master and Fellows of Gonville and Caius College, Cambridge, and the Council of the Middlesex Hospital Medical School. Under the terms of the bequest, medical centres in any part of the world may be visited with the exception of Oxford or Cambridge.

INSTITUTE OF NEUROLOGY

(Queen-square), London, W.C.1

(The National Hospital, Queen-square, and The Hospital for Nervous Diseases, Maida Vale)

A FULL-TIME COURSE IN CLINICAL NEUROLOGY will be held at The National Hospital, Queen-square, for 10 weeks beginning on 5TH OCTOBER, 1953, consisting of lectures and demonstrations in medical neurology, anatomy and physiology of the nervous system, methods of examination, neuro-pathology and psychology.

The lectures are given at 12 NOON and 2 P.M. daily, and arrangements can be made for students to attend these without entering for the full course.

Application should be made to The Dean, Institute of Neurology (Queen-square), The National Hospital, Queen-square, W.C.1.

UNIVERSITY OF LONDON POSTGRADUATE MEDICAL SCHOOL. Whole-time LECTURER IN ANÆSTHETICS. Salary range £1500–£2000 p.a. Required to combine practical demonstration of anæsthetics with interest in fundamental problems in relation to anæsthesia ; expected to help with administration of department.

Applications, with the names and addresses of 3 referees, to be submitted to the Dean, Postgraduate Medical School, Ducane-road, W.12, by 5th September, 1953.

THE WELSH NATIONAL SCHOOL OF MEDICINE

(UNIVERSITY OF WALES)

MORGAN E. WILLIAMS BEQUEST

Grants are available from the above Fund for award to medical practitioners and to non-medical men engaged in work of medical importance who are ordinarily resident in the County of Glamorgan.

The purpose of the Grant is to assist those wishing to travel abroad on short visits of medical interest.

Applications for Grants in 1954 must be received by the Secretary of the School, 34, Newport-road, Cardiff, from whom further particulars may be obtained, not later than 1st October, 1953.

Hospital Services : Senior Appointments

NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. PSYCHIATRIST (Consultant) required at the Child Guidance Training Centre, Osnaburgh-street, N.W.1, for 5 half-days a week. Wide experience in child psychiatry and teaching essential. Centre may be visited by direct appointment. Post vacant 1st January, 1954.

Detailed applications, including date of birth, and names of 3 referees, to Secretary, Central Middlesex Group Hospital Management Committee, Central Middlesex Hospital, Park Royal, N.W.10, by 29th August, 1953.

BIRMINGHAM REGIONAL HOSPITAL BOARD. Whole-time DEPUTY REGIONAL TRANSFUSION OFFICER (Regional Blood Transfusion Service). Salary scale £1300–£1750 p.a. Successful candidate will assist in supervision of laboratory activities and supervise donor sessions throughout region. Opportunity for research in hæmato-serology, hæmatology and bacteriology and for clinical experience. Previous experience in transfusion centre an advantage. Candidates with clinical pathology experience may apply.

Applications (15 copies), stating name, age, nationality, qualifications, present and previous appointments, and details of 3 referees, to Secretary, 10, Augustus-road, Birmingham, 15, before 17th August, 1953. Candidates may visit Centre by appointment with Regional Transfusion Officer, 15, Ampton-road, Birmingham, 15.

EAST ANGLIAN REGIONAL HOSPITAL BOARD. CONSULTANT PSYCHIATRIST (whole-time), Ipswich Mental Hospital Group—St. Clement's Hospital, Ipswich (400 Beds), and St. Audry's Hospital, Melton, near Woodbridge (900 Beds), and associated General Hospital outpatient clinics. Duties will be predominantly at St. Clement's and the outpatient clinics.

Applications (8 copies), stating age, qualifications, and details of present and previous appointments, together with names of 3 referees, to Secretary of Board, 117, Chesterton-road, Cambridge, by 17th August, 1953. Candidates invited to visit hospitals by direct arrangement with Medical Superintendent, St. Audry's Hospital.

LIVERPOOL REGIONAL HOSPITAL BOARD. SOUTHPORT AREA. Applications are invited for the post of VISITING CONSULTANT PHYSICIAN (part-time) for 4 notional half-days weekly. Duties mainly at Southport General Infirmary and Southport Promenade Hospital where the successful candidate will work with the existing Senior Visiting Physician. Applicants must possess a higher qualification in general medicine.

Forms of application from, and to be returned to, Dr. T. Lloyd Hughes, Senior Administrative Medical Officer, Liverpool Regional Hospital Board, 19, James-street, Liverpool, 2, to be received not later than 22nd August, 1953.

VINCENT COLLINGE, Secretary to the Board.

MANCHESTER REGIONAL HOSPITAL BOARD invite applications for the whole-time non-resident post of CONSULTANT RADIOTHERAPIST, Christie Hospital and Holt Radium Institute, Manchester. F.F.R. and a higher qualification in medicine or surgery will be additional advantages.

Application forms from the Senior Administrative Medical Officer to the Board at Cheetwood-road, Manchester, 8, to be returned by 17th August, 1953.

NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. ASSISTANT ORTHOPÆDIC AND ACCIDENT SURGEON (Consultant status) required at Luton and Dunstable Hospital, where there is a well-developed Accident Service covering much of Bedfordshire and including Hitchin. The Hospital has 250 Beds, including 50 for orthopædic and accident cases. Post will be whole-time but 5 years from date of taking up duty the holder will be given free choice of transferring to maximum sessions if he so desires. Hospital may be visited by direct appointment.

Detailed applications, including date of birth, and names of 3 referees, to Secretary, North West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 5th September, 1953.

SHEFFIELD REGIONAL HOSPITAL BOARD. CONSULTANT SURGEON required for 8 notional half-days per week. Duties at Beckett Hospital, Barnsley, and City General Hospital, Sheffield.

Application forms obtainable from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 29th August, 1953.

SHEFFIELD REGIONAL HOSPITAL BOARD/UNITED SHEFFIELD HOSPITALS. Maximum Part-time CONSULTANT E.N.T. SURGEON required to undertake 5 notional half-days per week for the Sheffield Regional Hospital Board and 4 notional half-days per week in The United Sheffield Hospitals. Regional Board duties at Chesterfield and Sheffield.

Applications to the Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, from whom application forms and full details may be obtained. Completed forms to be returned by 22nd August, 1953.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time Locum ASSISTANT RADIOTHERAPIST required immediately at the Derbyshire Royal Infirmary for a period of approximately 4–6 months. Remuneration at the rate of 31½ guineas per week.

Apply to the Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, naming 2 referees.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time SENIOR ASSISTANT PSYCHIATRIST required for the Towers Hospital, Humberstone, near Leicester. A 7-room flat is available. Salary £1300–£50–£1750.

Application forms obtainable from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 22nd August, 1953.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of Part-time (9 sessions) ASSISTANT ORTHOPÆDIC SURGEON of Consultant status for the Orthopædic Service in Edinburgh. The person appointed may be required to undertake his main duties in either the Royal Infirmary of Edinburgh or the Princess Margaret Rose Hospital, and in either instance will be required to assist in other hospitals in Edinburgh and to take part in the staffing of certain peripheral clinics. The post is superannuable, and the conditions of service are in accordance with the regulations.

Applications, giving particulars of age, previous experience and qualifications, together with the names of 3 referees, should be submitted to the Secretary, South-Eastern Regional Hospital Board, Scotland, 11, Drumsheugh-gardens, Edinburgh, 3, by 31st August.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited for a post of TUBERCULOSIS PHYSICIAN at the Victoria Hospital, Kirkcaldy. The appointment involves the conduct of outpatient and domiciliary work in the Eastern part of the County of Fife and the care of some 50 tuberculosis beds in the Victoria Hospital. The general supervision of the Tuberculosis Service is exercised by the Consultant Physician-Superintendent of Glenlomond Sanatorium. The post is on the salary scale £1300–£50–£1750. The post is superannuable and the conditions of service are in accordance with the regulations.

Applications, giving particulars of age, qualifications, and previous experience, together with the names of 3 referees, should be submitted to the Secretary, South-Eastern Regional Hospital Board, Scotland, 11, Drumsheugh-gardens, Edinburgh, 3, by 31st August.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires Whole-time ASSISTANT PATHOLOGIST (Senior Hospital Medical Officer grade) for the Kingston (Surrey) Group Laboratory. Experience in all branches of clinical pathology desirable but principal duties will be in hæmatology.

Applications (5 copies), giving date of birth, qualifications, experience, names of 3 referees, to Secretary (S.1), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 22nd August, 1953. Applicants may visit Laboratory by local arrangement.

NORTHERN IRELAND HOSPITALS AUTHORITY invite applications for the whole-time post of MEDICAL BIOCHEMIST, in the grade of Senior Hospital Medical Officer, to the Authority's Central Laboratory, 51, Lisburn-road, Belfast. The person appointed will be responsible to the Consultant Pathologist in charge of the Laboratory. The terms, conditions of service, and remuneration for the post will be in accordance with the Authority's application of the Spens Report to Northern Ireland.

Applications should be made on a form which may be obtained from the Secretary, Northern Ireland Hospitals Authority, Friends' Provident Building, 58, Howard-street, Belfast, and which must be returned to him so as to be received not later than 15th August, 1953.

NEWFOUNDLAND. WEST COAST SANATORIUM, CORNER BROOK. The above Hospital, for the treatment of tuberculosis, requires an ASSISTANT SUPERINTENDENT, a permanent and pensionable position. The salary is $8000 p.a. and the Hospital is a new one, having been opened in 1951. It has a capacity of 270 Beds, is fully equipped for diagnostic, medical, and surgical services, and operates a large Outpatient Department. An unfurnished, modern home is available, at a rental of $50 monthly, deductable from the salary. The town of Corner Brook, in Western Newfoundland, has a population of 20,000 and recreational facilities include golf, fishing, hunting, as well as all types of winter sports.

Applications, including qualifications and experience, should be addressed to E. S. Peters, M.D., C.M., Superintendent, West Coast Sanatorium, Corner Brook.

LEONARD MILLER, M.D., Deputy Minister of Health.

Hospital Services : Junior Appointments

BROMPTON HOSPITAL, S.W.3. Applications are invited for the post of NON-RESIDENT HOUSE PHYSICIAN for which there are 3 vacancies, for 6 months from 1st October. Duties include work in Outpatient Department and wards. Salary £400 or £450 a year, according to experience.

Applications, stating age, qualifications with dates, nationality and appointments held, together with copies of testimonials, by 8th August, to KENNETH A. F. MILES, House Governor.

BATTERSEA GENERAL HOSPITAL, Battersea Park, S.W.11. CASUALTY OFFICER/HOUSE SURGEON (resident). House Officer or Senior House Officer grade, according to experience. Vacant early August.

Apply, enclosing copies of 2 recent testimonials, to Hospital Secretary.

EVELINA CHILDREN'S HOSPITAL OF GUY'S HOSPITAL, Southwark Bridge-road, London, S.E.1. Locum RESIDENT CASUALTY OFFICER (House Officer grade) from 17th August, to 31st October, 1953.

Applications to Hospital Secretary immediately.

ELIZABETH GARRETT ANDERSON HOSPITAL, Euston-road, N.W.1. (ROYAL FREE HOSPITAL GROUP.) Applications are invited from pre-registration and registered Women medical practitioners for the post of HOUSE SURGEON to Gynæcological Department (recognised for M.R.C.O.G.). Duties to commence 1st September, 1953. Appointment for 6 months. Salary in accordance with Ministry of Health scale for House Officers.

Applications, with copies of 3 recent testimonials, to be sent to the Secretary, Elizabeth Garrett Anderson Hospital, as soon as possible.

ELIZABETH GARRETT ANDERSON HOSPITAL, Euston-road, N.W.1. (ROYAL FREE HOSPITAL GROUP.) Applications are invited from pre-registration and registered Women medical practitioners for the post of SECOND HOUSE SURGEON/CASUALTY OFFICER, with duties in Gynæcological and Special Departments. Appointment for 6 months from 1st October, 1953. Salary according to Ministry of Health scale for House Officers.

Applications, with copies of 3 recent testimonials, should be sent to the Secretary, Elizabeth Garrett Anderson Hospital, by 13th August, 1953.

FOREST GATE HOSPITAL, Forest-lane, E.7. Applications are invited for the resident post of HOUSE OFFICER (obstetrics—second or third post). The appointment is for 6 months, commencing 1st September, 1953, and is recognised for the training of candidates for D.Obst.R.C.O.G.

Written applications, together with 2 references, should be received by the Group Secretary, West Ham Group Hospital Management Committee, Stratford, E.15, not later than 6th August, 1953.

GERMAN HOSPITAL, Dalston, London, E.8. (General.) Applications are invited for the appointment of HOUSE SURGEON for a period of 6 months, and should be sent to the Group Secretary, Hackney Hospital Management Committee, London, E.9, by 10th August, quoting reference GH/HS.

GERMAN HOSPITAL, Dalston, London, E.8. (General—153 Beds.) Applications are invited for the 12 months appointment of CASUALTY OFFICER with anæsthetic duties (Senior House Officer grade), which is vacant at end of August.

Apply Group Secretary, Hackney Hospital Management Committee, E.9, by 10th August, quoting reference GH/SHO.

HAMMERSMITH HOSPITAL AND POSTGRADUATE MEDICAL SCHOOL, Ducane-road, London, W.12. CASUALTY OFFICER (non-resident) required 1st September. Salary £670 p.a.

Applications, stating age, qualifications, experience, copies of 2 recent testimonials, to Secretary, Board of Governors, by 10th August.

HAMMERSMITH HOSPITAL AND POSTGRADUATE MEDICAL SCHOOL, London, W.12. HOUSE SURGEON (orthopædics) required immediately.

Applications, stating age, qualifications, experience, copies of 2 recent testimonials, to Secretary, Board of Governors.

HAMMERSMITH HOSPITAL AND POSTGRADUATE MEDICAL SCHOOL, London, W.12. BLOOD TRANSFUSION OFFICER (Registrar grade), resident or part-resident, required for 1 year from 1st October. Opportunities for research.

Applications, stating age, qualifications, experience, copies of 2 testimonials, to Secretary, Board of Governors, by 15th August.

HACKNEY HOSPITAL, E.9. (811 Beds.) Applications are invited for second or third post CASUALTY HOUSE OFFICER, to act also as House Physician to the Skin Department. 6 months appointment.

Applications, with 3 testimonials, to the Secretary, Hospital Management Committee, Hackney Hospital, E.9.

HACKNEY HOSPITAL, London, E.9. (General—811 Beds.) Applications are invited for the 6 months appointment of HOUSE PHYSICIAN, vacant on 8th September, and should be sent to the Group Secretary, Hackney Hospital Management Committee, E.9, by 17th August, quoting reference HH/HP.

LONDON CHEST HOSPITAL. Hospitals for Diseases OF THE CHEST. 2 vacancies occur 1st October, 1953, for RESIDENT HOUSE PHYSICIAN. Appointments for 6 months, 4 in London, 2 at the Country Branch, near Letchworth, and posts are graded as House Officer. Duties include work in the Outpatient Department and Refill Clinic as well as in wards.

Applications, stating age, qualifications with dates, and previous appointments held, with copies of 3 testimonials, should reach the undersigned not later than 21st August.

THOMAS BROWN, House Governor.

London Chest Hospital, E.2.

LONDON CHEST HOSPITAL. Hospitals for Diseases OF THE CHEST. A vacancy occurs 1st October, 1953, for RESIDENT SURGICAL OFFICER. Appointment for 6 months, with prospect of renewal, of which 2 will be at the Country Branch, near Letchworth. Post graded as Senior House Officer or Registrar, according to qualifications and experience. Previous surgical experience necessary.

Applications, stating age, qualifications with dates, and previous appointments held, with copies of 3 testimonials, should reach the undersigned not later than 21st August.

THOMAS BROWN, House Governor.

London Chest Hospital, E.2.

LONDON CHEST HOSPITAL. Hospitals for Diseases OF THE CHEST. Applications are invited for the appointment of Part-time MEDICAL REGISTRAR (grading : Senior Registrar). The duties require the equivalent of 5 notional half-days a week, including 1 Refill Clinic. The appointment is for 1 year and is renewable.

Applications, stating age, qualifications with dates, and previous appointments held, and accompanied by copies of 3 testimonials, should reach the undersigned not later than 21st August. THOMAS BROWN, House Governor.

London Chest Hospital, E.2.

LAMBETH HOSPITAL, Brook-drive, S.E.11. Applications are invited from pre-registration and registered medical practitioners for the positions (2) of RESIDENT HOUSE SURGEON. The appointments are for 6 months, commencing on 11th August, 1953, and are recognised for the F.R.C.S.

Application forms may be obtained from the Physician-Superintendent at the Hospital.

LONDON JEWISH HOSPITAL, Stepney Green, London, E.1. Applications are invited for the post of RESIDENT HOUSE PHYSICIAN, vacant 9th August, 1953. Tenable for 6 months, renewable. (Available as pre-registration appointment.) Salary £350, £400, or £450 p.a. according to experience, subject to deduction at the rate of £100 p.a. for board, lodging, &c.

Applications, with copies of testimonials, to the Secretary, London Jewish Hospital.

MARIE CURIE HOSPITAL, 66, Fitzjohn's-avenue, Hampstead, N.W.3. Applications are invited from registered medical practitioners for the post of GYNÆCOLOGICAL HOUSE SURGEON (radiotherapy). Vacant immediately.

Application with copies of testimonials to the Medical Director.

NORTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD.

(1) Part-time REGISTRAR in Thoracic Surgery (non-resident), North Middlesex Hospital, Edmonton, N.18. F.R.C.S. essential. 4 sessions a week on 4 separate days.

(2) REGISTRAR in Medicine (resident), St. Michael's Hospital, Braintree, Essex.

(3) REGISTRARS in Medicine (2 posts—resident), Tilbury and Riverside General and Thurrock Hospitals. Single accommodation available. Non-residence may be considered. Applicants will be interchangeable in the Orsett, Tilbury, and Thurrock Hospitals to gain widest experience in all phases of medicine, including infectious diseases and tuberculosis.

(4) MEDICAL REGISTRAR (pulmonary tuberculosis), resident, Broomfield Hospital, near Chelmsford, Essex (300 Beds). Some experience of diagnosis and treatment of pulmonary tuberculosis desirable. Post offers experience of all forms of modern therapy together with mass radiography and chest clinic services, and duties involve primarily work with Thoracic Surgeons.

(5) REGISTRAR in Pathology (non-resident), Tottenham Group Laboratory with duties mainly at St. Ann's General Hospital.

(6) E.N.T. REGISTRAR (non-resident), Whipps Cross Hospital, London, E.11.

(7) REGISTRAR in Anæsthetics (non-resident), North Middlesex Hospital and Annexes, Edmonton, N.18. Recognised for D.A.

(8) REGISTRAR in Anæsthetics (resident), Bethnal Green Hospital, Cambridge Heath-road, E.2. Recognised for D.A.

(9) REGISTRAR in Anæsthetics (resident preferred), Harold Wood Hospital, Harold Wood, Essex.

(10) REGISTRAR in General Surgery (non-resident), Hertford County Hospital, Hertford.

(11) REGISTRAR in Surgery (non-resident), Chelmsford and Essex Hospital. Duties are mainly at the above Hospital.

Appointments subject to review after 1 year.

Separate applications in duplicate, detailing date of birth, qualifications, experience, present appointment, grade and salary, with 2 copies of 2 recent testimonials, to Secretary, 11A, Portland-place, W.1, by 15th August, 1953.

NELSON HOSPITAL, Kingston-road, Merton, S.W.20. ST. HELIER GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of HOUSE SURGEON (approved pre-registration post) falling vacant 10th August.

Applications, stating age, qualifications, with the names and addresses of 2 referees, to be sent to the Group Secretary, St. Helier Hospital, Carshalton, Surrey.

NELSON HOSPITAL, Kingston-road, Merton Park, S.W.20. ST. HELIER GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for appointment of RESIDENT HOUSE SURGEON, vacant now. Salary £350–£450 p.a. according to experience. Post recognised for F.R.C.S.

Applications, stating age, experience and qualifications, with copies of 2 testimonials, and the name of 1 referee, should be sent immediately to the Group Secretary, St. Helier Hospital, Carshalton, Surrey.

NELSON HOSPITAL, Kingston-road, Merton Park, S.W.20. ST. HELIER GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of SENIOR HOUSE OFFICER (Casualty Officer). Post vacant. Salary £670 p.a., less £150 p.a. for residential emoluments.

Applications, together with copies of 2 testimonials and the name and address of 1 referee, should be sent to the Group Secretary, St. Helier Hospital, Carshalton, Surrey.

PADDINGTON GREEN CHILDREN'S HOSPITAL, W.2. (ST. MARY'S HOSPITAL.) Applications are invited for the post of CASUALTY OFFICER (third post). Non-resident appointment, House Officer grade, tenable for 6 months, as from 1st October, 1953.

Applications, stating age, nationality, qualifications with dates, and experience, with copies of 3 recent testimonials, should reach the Secretary not later than 15th August, 1953.

SPRINGFIELD HOSPITAL MANAGEMENT COMMITTEE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR required. The Hospital is a large one and offers excellent experience in diagnosis and treatment of all forms of mental disorder including the neuroses. Every variety of modern treatment is carried out in a well-equipped treatment centre. Single accommodation available for which a deduction of £130 p.a. will be made. Candidates may visit the Hospital by arrangement.

Apply to Secretary, Springfield Hospital, Beechcroft-road, Upper Tooting, S.W.17, for application forms which should be returned, duly completed, on or before 15th August, 1953.

PRINCESS BEATRICE HOSPITAL, Earl's Court, S.W.5. HOUSE PHYSICIAN (some casualty work), registered practitioner, 6 months appointment from 1st September, preceded by 1 weeks Locum from 24th August.

Applications, with 3 testimonials, to the House Governor by 14th August.

PRINCE OF WALES'S GENERAL HOSPITAL, N.15. (219 Beds.) TOTTENHAM GROUP HOSPITAL MANAGEMENT COMMITTEE (GROUP 4). Applications are invited from registered medical practitioners for the appointment of SENIOR HOUSE OFFICER RESIDENT ANÆSTHETIST, for a period of 6 months, vacant immediately.

Application form from Secretary, to be returned at once.

ROYAL CANCER HOSPITAL, Fulham-road, London, S.W.3. Applications are invited for the post of Full-time REGISTRAR in the Radiotherapy Department to commence duty as soon as possible. Candidates should hold a Diploma in Medical Radiology.

Forms of application are obtainable from the House Governor to whom applications, together with copies of 3 recent testimonials, should be sent not later than 24th August, 1953.

ROYAL FREE HOSPITAL. Applications are invited from registered medical practitioners for the post of RESIDENT CASUALTY OFFICER. Applicants must not be more than 10 years qualified. The appointment is for 6 months, duties to commence on 1st September, 1953. Salary and conditions of service in accordance with those laid down by the Ministry of Health for Senior House Officers.

Application forms may be obtained from the Secretary to the Board of Governors, The Royal Free Hospital, Gray's Inn-road, London, W.C.1, to whom they should be returned not later than 8th August, 1953.

ROYAL NORTHERN HOSPITAL, Holloway, N.7. Applications are invited for the post of SENIOR HOUSE OFFICER (orthopædics), vacant 24th August, 1953. Occasional casualty duties involved.

Applications, stating age, qualifications, and experience, with copies of recent testimonials, to be sent to the Hospital Secretary by 8th August, 1953.

ROYAL NORTHERN HOSPITAL, Holloway, N.7. Applications are invited for the post of HOUSE SURGEON, vacant 1st September, 1953. Preference given to candidates seeking pre-registration posts under the Medical Act, 1950.

Applications, stating age, qualifications and experience, with copies of recent testimonials, to be sent to the Hospital Secretary by 8th August, 1953.

ROYAL NORTHERN HOSPITAL, Holloway, N.7. Applications are invited for the post of SECOND RESIDENT ANÆSTHETIST (Senior House Officer grade), vacant 16th September, 1953. Salary £670 p.a., less £130 p.a. board-residence. Appointment recognised for D.A.

Applications, stating age, qualifications, and experience, with copies of recent testimonials, to be sent to the Hospital Secretary by 8th August, 1953.

ROYAL NATIONAL ORTHOPÆDIC HOSPITAL, 234, Great Portland-street, W.1. Applications are invited for the appointments of 3 SENIOR ORTHOPÆDIC REGISTRARS (full-time, non-resident). Applicants must be Fellows of 1 of the Royal Colleges of Surgeons. 2 to commence duties 1st November and 1 on 1st December, 1953.

Applications to be received not later than 3rd September. Form of application can be obtained from the House Governor at 234, Great Portland-street, London, W.1.

ROYAL NATIONAL ORTHOPÆDIC HOSPITAL, 234, Great Portland-street, London, W.1. Applications are invited for the appointments of 2 or 3 ORTHOPÆDIC REGISTRARS (full-time, non-resident). Duties to commence 1st November, 1953. Applications to be received not later than 3rd September. Preference will be given to candidates with a higher surgical qualification.

Form of application can be obtained from the House Governor at 234, Great Portland-street, London, W.1.

ST. GILES' HOSPITAL, Camberwell, London, S.E.5. CAMBERWELL HOSPITALS MANAGEMENT COMMITTEE. Applications invited for appointment as HOUSE OFFICER (duties: obstetrics and gynæcology). Salary £350, £400, or £450 a year, according to posts held, with deduction at the rate of £100 a year in respect of residence. Recognised pre-registration post. Vacant from 1st September, 1953.

Applications, stating age, qualifications, previous posts, if any, with copy testimonials or names of referees, to the Group Secretary, Camberwell Hospitals Management Committee, Dulwich Hospital, East Dulwich-grove, S.E.22.

ST. LEONARD'S HOSPITAL, Nuttall-street, London, N.1. (Acute General—182 Beds.) Applications are invited from registered medical practitioners for the post of SENIOR HOUSE OFFICER (casualty), tenure 1 year. Salary £670 p.a., less £130 p.a. residential charges.

Applications, stating age, qualifications, experience, &c., with names of 3 referees, to the Hospital Secretary immediately.

ST. ANN'S GENERAL HOSPITAL, N.15. (756 Beds.) Applications are invited from registered medical practitioners for the appointment of RESIDENT HOUSE PHYSICIAN (Senior House Officer) for duty in the Infectious Diseases Unit and other general duties, for a period of 6 months commencing 4th September, 1953.

Application form from Secretary, Tottenham Group Hospital Management Committee, The Green, Tottenham, N.15, to be returned by 22nd August, 1953.

ST. THOMAS'S HOSPITAL, London, S.E.1. Senior REGISTRAR to the Department of Physical Medicine for 1 year in the first instance, from 1st October, 1953. D.Phys.Med. essential.

Applications, including names and addresses of 2 referees, to the Clerk of the Governors by 16th August, 1953.

SOUTH WESTERN HOSPITAL, Landor-road, S.W.9. RESIDENT SURGICAL OFFICER (Senior House Officer grade) required to take charge of 32 surgical beds which are under the direction of the Surgical Consultant of Lambeth Hospital, Kennington; and also to work under the E.N.T. Consultant at the South Western Hospital.

For form of application apply to the Group Secretary, Lambeth Group Hospital Management Committee, Renfrew-road, S.E.11.

WESTMINSTER HOSPITAL, St. John's-gardens, S.W.1. Applications invited for post of SENIOR HOUSE OFFICER to E.N.T. Department starting 1st September. Appointment for 1 year.

Applications (6 copies), with names of 2 referees, to House Governor as soon as possible.

WESTMINSTER HOSPITAL, St. John's-gardens, S.W.1. Applications invited from registered medical practitioners for appointment of SENIOR REGISTRAR to Psychiatric Department for 1 year in first instance starting mid-October or earlier if possible. Candidates must hold the D.P.M.

Applications (7 copies), with names of 2 referees, to House Governor by 15th August.

WHIPPS CROSS HOSPITAL, London, E.11. Leytonstone NO. 10 HOSPITAL GROUP. Required at above Hospital, Temporary TUBERCULOSIS REGISTRAR. The permanent establishment of the Tuberculosis Unit to be reviewed in December, 1953.

Further particulars and application forms from the Hospital Secretary, Whipps Cross Hospital, London, E.11 (LEYtonstone 5522). Application forms to be returned by 14th August.

WIMBLEDON HOSPITAL, Thurstan-road, Wimbledon, S.W.20. ST. HELIER GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT HOUSE OFFICER with duties in medicine, surgery and pædiatrics. Salary £350–£450 p.a. according to experience. Now vacant.

Applications, stating age, qualifications and experience, with copies of 2 testimonials, and the name and address of 1 referee, should be sent to the Group Secretary, St. Helier Hospital, Carshalton, Surrey.

AYLESBURY. ROYAL BUCKINGHAMSHIRE AND ASSOCIATED HOSPITALS MANAGEMENT COMMITTEE. Applications are invited for the following appointments:—

Royal Buckinghamshire Hospital

SENIOR HOUSE OFFICER to Accident and Orthopædic Department, vacant now. Duties include charge of Casualty Department, together with those of Senior Resident. Salary £670 p.a., less £140 p.a. for residence, &c.

SENIOR HOUSE OFFICER for Accident and Orthopædic Department (which is centred upon this Hospital and comprises 48 Beds), vacant 1st August.

Applications for both appointments, with 2 testimonials, to Secretary-Superintendent as soon as possible.

Stoke Mandeville Hospital

SENIOR HOUSE OFFICER (pathology) for a busy and expanding laboratory situated at the above Hospital, in which all branches of clinical pathology for over 1000 Beds are undertaken. Salary £670 p.a. Single accommodation is available at charge of £140 p.a.

Applications with copies of 2 testimonials to the Administrative Officer as soon as possible.

Tindal General Hospital

HOUSE SURGEON (E.N.T.), Male or Female, vacant now. New department with high turnover and 4 Outpatient Clinics weekly. No casualty department. Recognised for F.R.C.S. and D.L.O. Applications for locum appointment will be considered.

HOUSE PHYSICIAN (Chest Unit), second or third post, Male or Female, vacant 1st September. Duties include care of about 20 chest cases (including T.B. Chalets) which may increase in due course, and 4 clinics weekly, including refills, forming a progressive chest unit for the Aylesbury area. Instruction in bronchoscopy and bronchography given. An acute Geriatric Unit, a small long-stay Annexe and a medical Outpatient Clinic provide some general medicine. No casualty department.

Both posts are recognised for Pre-registration Service, but registered practitioners are invited to apply.

Applications, with 2 testimonials, to the Administrative Officer as soon as possible.

ASHFORD HOSPITAL, Ashford, Kent. Applications are invited from medical practitioners for the post of RESIDENT HOUSE PHYSICIAN at the above Hospital. Salary £350, £400, or £450 a year according to experience. A deduction of £100 a year will be made in respect of residential emoluments.

Applications, stating age, qualifications, and the names and addresses of 2 referees, to the Group Secretary, "Ash-Eton," Radnor Park West, Folkestone.

ASHFORD (near), KENT. WILLESBOROUGH HOS-PITAL. Applications are invited for the appointment of HOUSE PHYSICIAN at the above Hospital. Salary £350, £400, or £450 a year according to experience. A deduction of £100 a year will be made in respect of residential emoluments.

Applications, stating age, qualifications, and the names and addresses of 2 referees, to the Group Secretary, "Ash-Eton," Radnor Park West, Folkestone.

ASHFORD (near), KENT. WILLESBOROUGH HOS-PITAL. Applications are invited for the appointment of HOUSE SURGEON at the above Hospital. Good experience in general surgery with some casualty work. Salary £350, £400, or £450 a year, less £100 a year for residential emoluments.

Applications, stating age, qualifications, and the names and addresses of 2 referees, should be forwarded to the Group Secretary, "Ash-Eton," Radnor Park West, Folkestone.

BARNSLEY. ST. HELEN HOSPITAL. Locum Medical OFFICER for general and pædiatric wards required 18th September–2nd October (inclusive). Salary £16 per week.

Apply: Group Secretary, Barnsley Hospital Management Committee, 33 Gawber-road, Barnsley.

ABERDEEN ROYAL INFIRMARY. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER in General Medicine. Conditions of service in accordance with the terms issued by the Department of Health for Scotland.

Applications, with the names of 2 referees, to be lodged with the Secretary, Aberdeen General Hospitals, 62, Queen's-road, Aberdeen, within 14 days of the appearance of this advertisement.

ASHTON, HYDE AND GLOSSOP HOSPITAL MANAGE-MENT COMMITTEE. Applications are invited for the post of HOUSE SURGEON at Ashton-under-Lyne General Hospital (800 Beds), vacant now. Preference will be given to pre-registration applicants.

Applications, giving age, nationality, qualifications, and experience, with copies of 3 testimonials, should be forwarded to the Group Secretary, Astley-road, Stalybridge, Cheshire, as soon as possible.

AYRSHIRE. BALLOCHMYLE HOSPITAL, Mauchline. (346 Beds.) JUNIOR HOSPITAL MEDICAL OFFICER (plastic surgery and maxillo-facial unit). New appointment. Resident. National terms. Offers a wide variety of experience in all aspects of plastic surgery, oral surgery and the treatment of burns.

Apply immediately to Area Medical Superintendent, Ballochmyle Hospital, Mauchline, giving the names of 2 referees.

BARRY ACCIDENT AND SURGICAL HOSPITAL. CARDIFF HOSPITAL MANAGEMENT COMMITTEE. HOUSE OFFICER (but may be Senior House Officer if sufficient experience) required immediately at above Hospital. Staffed by whole-time Consultant Surgeon and Surgical Registrar. Excellent experience given in general surgery.

Form of application from Group Secretary, 44, Cathedral-road, Cardiff.

BARROW-IN-FURNESS. NORTH LONSDALE HOS-PITAL. BARROW AND FURNESS HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for resident posts of SENIOR HOUSE SURGEON and HOUSE SURGEON (recognised for pre-registration) at the above Hospital, with surgical work under control of Consultant Surgeons. Posts recognised for F.R.C.S. National conditions and salary scales.

Applications to the Secretary of the Committee, 52, Paradise-street, Barrow-in-Furness.

BEDFORD GENERAL HOSPITAL. (435 Beds.) Bedford GROUP HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (Male or Female) in Obstetrics and Gynæcology, required to be resident at the Bedford General Hospital (North Wing). The Unit comprises 59 obstetric and 20 gynæcological beds and a busy Outpatient Department, offering excellent experience. Post vacant 20th September, 1953, and recognised for the D.Obst.R.C.O.G. Salary £670 p.a., less £130 for emoluments.

Application forms obtainable from, and returnable to, Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford, by 19th August, 1953.

BEDFORD GENERAL HOSPITAL. (435 Beds.) Bedford GROUP HOSPITAL MANAGEMENT COMMITTEE. RESIDENT HOUSE SURGEON required immediately. This is a new appointment for duties principally in the E.N.T. and Ophthalmic Departments.

Applications, stating age, nationality, qualifications, previous appointments, together with copies of 2 testimonials, should be forwarded to the Group Secretary, 3, Kimbolton-road, Bedford.

BEXHILL-ON-SEA. BEXHILL HOSPITAL. (62 Beds.) 2 HOUSE SURGEONS. Posts now vacant. (A small modern hospital on the South coast.) Considerable acute surgical work and busy Outpatient Department. Excellent all-round experience. National scale of salary.

Apply to Hospital Administrator.

BIRMINGHAM. LORDSWOOD MATERNITY HOS-PITAL, Lordswood-road, HARBORNE, BIRMINGHAM, 17. Applications are invited for the post of RESIDENT OBSTETRIC HOUSE OFFICER. The appointment is for a period of 6 months commencing 1st September, 1953. The Hospital has 33 Beds dealing with normal and abnormal midwifery. Appointment recognised for D.Obst.R.C.O.G. Second period Training School for Pupil Midwives.

Applications to be addressed to the Obstetrician.

BIRMINGHAM, 29. SELLY OAK HOSPITAL. (1059 Beds.) Applications are invited for the post of CASUALTY OFFICER (Senior House Officer), resident or non-resident. Available immediately.

Apply, giving qualifications, experience and age, with copies of 3 testimonials, to the Medical Superintendent.

BIRMINGHAM, 23. HIGHCROFT HALL HOSPITAL. Applications are invited for the following appointments at the above Mental Hospital (1227 Beds).

RESIDENT SENIOR HOUSE OFFICER (Male or Female). The Hospital has modern admission-units and all forms of psychiatric treatment are undertaken. It serves an extensive area of North Birmingham and Sutton Coldfield and a large amount of outpatient work is carried out in the clinics attached to the Hospital. Opportunities are available for postgraduate studies.

JUNIOR HOSPITAL MEDICAL OFFICER (Locum), Male or Female. Accommodation available, but Officer who so desires may live outside the Hospital.

Applications, giving full particulars should be addressed to the Medical Superintendent.

BIRMINGHAM, 18. DUDLEY ROAD INFIRMARY, Western-road. JUNIOR HOSPITAL MEDICAL OFFICERS required. The Hospital has 1000 Beds for the care of the chronic sick and an active Geriatric Unit. Salary £700–£1000 p.a.

Applications, with copies of 3 recent testimonials, to Secretary, Hospital Management Committee, Dudley Road Hospital, Birmingham, 18.

BIRMINGHAM REGIONAL HOSPITAL BOARD.

(*a*) **Wolverhampton, Royal Hospital**

Whole-time RESIDENT REGISTRAR in Anæsthetics.

(*b*) **Biddulph Grange Orthopædic Hospital, Stoke-on-Trent** (104 children's beds)

Whole-time REGISTRAR in Orthopædics. Extensive experience in long-stay cases available. Resident.

(*c*) **North Staffordshire Royal Infirmary, Stoke-on-Trent** (475 Beds—66 traumatic)

Whole-time REGISTRAR in Orthopædics. Duties also at Orthopædic Hospital (77 Beds). Resident or non-resident. Experience specialty essential. Higher qualification an advantage.

(*d*) **Stafford. St. George's Hospital** (1334 Beds)

Whole-time REGISTRAR in Psychiatry. Single or married accommodation available. Experience specialty essential. Possession of higher qualification an advantage. Recognised for D.P.M.

(*e*) **Stoke-on-Trent Group of hospitals**

Whole-time REGISTRAR in Thoracic Surgery. Duties at Chest Unit, Cheshire Joint Sanatorium (305 Beds), and North Staffs Royal Infirmary (475 Beds). Experience general surgery essential. Higher surgical qualification an advantage.

(*f*) **Birmingham (Dudley Road) Group of hospitals**

Whole-time REGISTRAR in Obstetrics and Gynæcology. Duties at Marston Green Maternity Hospital (126 obstetric and 10 gynæcological beds). Recognised for obstetric part of M.R.C.O.G. and affiliated to Birmingham Medical School for training of students. Resident. Experience specialty essential.

Application forms from Secretary, 10, Augustus-road, Birmingham, 15, before 17th August, 1953.

BIRMINGHAM (near). MARSTON GREEN MATERNITY HOSPITAL, Berwicks-lane, MARSTON GREEN, near BIRMINGHAM. HOUSE SURGEON (obstetrics) required. Post vacant 1st September, 1953. 126 obstetric and 10 gynæcological beds. Post recognised for diploma and obstetric part of Membership of Royal College of Obstetricians and Gynæcologists. Hospital affiliated to Birmingham Medical School for training of students.

Detailed applications, accompanied by copies of 3 recent testimonials to the Secretary, Hospital Management Committee, Dudley Road Hospital, Birmingham, 18.

BIRMINGHAM (SANATORIA) GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER at West Heath Sanatorium, Rednal-road, Birmingham, 31 (210 Beds). The successful applicant will reside at the above Sanatorium (accommodation for single person only), and will be required to undertake duties at the Birmingham Chest Clinic, Great Charles-street, Birmingham, 3.

Applications, stating age, qualifications, training and experience, together with copies of 3 recent testimonials, should be addressed to the Secretary, Birmingham (Sanatoria) Group Hospital Management Committee, Yardley Green Hospital, Birmingham, 9, as soon as possible.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. Applications are invited for the post of RESIDENT ANÆSTHETIST (Senior House Officer grade), for duties within the Teaching Group, and resident at the Queen Elizabeth Hospital. Vacant 1st October and tenable for 1 year. The appointment is a recognised post for the purpose of taking the F.F.A.R.C.S. examination.

Application forms may be obtained from the Secretary, United Birmingham Hospitals, Queen Elizabeth Hospital, Birmingham, 15, and should be returned to him not later than 22nd August, 1953.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. Applications are invited for the temporary appointment of RESIDENT REGISTRAR in Anæsthetics (Registrar grade). The appointment is a temporary one for a period of 6 months, from 1st October, 1953. The successful candidate will be resident at the Queen Elizabeth Hospital but will be required to undertake duties at other hospitals within the Teaching Group. Preference will be given to candidates who have passed the Part I examination for the Diploma in Anæsthetics.

Application forms may be obtained from the Secretary, United Birmingham Hospitals, Queen Elizabeth Hospital, Birmingham, 15, and should be returned to him not later than 22nd August, 1953.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. Applications are invited for the post of RESIDENT CLINICAL PATHOLOGIST (Senior House Officer grade) in the Department of Bacteriology and Clinical Pathology at the General Hospital. The appointment is tenable for 12 months.

Application forms may be obtained from the Secretary, United Birmingham Hospitals, Queen Elizabeth Hospital, Birmingham, 15, and should be returned to him as soon as possible.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. Applications are invited for the appointment of SENIOR HOUSE OFFICER (E.N.T. Department), non-resident, for duties within the constituent hospitals of the Teaching Group. Some previous experience in the specialty desirable.

Forms of application may be obtained from the Secretary, United Birmingham Hospitals, Queen Elizabeth Hospital, Birmingham, 15, and should be returned not later than 15th August, 1953.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. Applications are invited for the appointment of REGISTRAR (E.N.T. Department), non-resident, for duties within the constituent hospitals of the Teaching Group, including the Children's Hospital, and to commence on 1st September, 1953. Preference will be given to applicants with previous experience in the specialty.

Forms of application may be obtained from the Secretary, United Birmingham Hospitals, Queen Elizabeth Hospital, Edgbaston, Birmingham, 15, and should be returned not later than 15th August, 1953.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. THE QUEEN ELIZABETH HOSPITAL. Applications are invited for the post of RESIDENT OBSTETRIC AND GYNÆCOLOGICAL REGISTRAR, for duties at the Queen Elizabeth Hospital (Professorial Unit) to commence 1st October, 1953.

Forms of application with details of appointment, may be obtained from, and should be returned not later than 22nd August, 1953, to, the Secretary, United Birmingham Hospitals, Queen Elizabeth Hospital, Birmingham, 15.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. THE CHILDREN'S HOSPITAL, Ladywood-road, BIRMINGHAM, 16. SENIOR HOUSE OFFICER (casualty) required to commence duty on 1st October, 1953. Previous surgical experience essential.

Forms of application may be obtained from the House Governor, and should be returned not later than 22nd August, 1953. G. A. PHALP, Secretary to the Board of Governors.

BISHOP'S STORTFORD, HERTS. HAYMEADS HOSPITAL. (400 occupied beds. Midway between London and Cambridge. Main Line Railway from Liverpool Street.) Applications are invited from registered medical practitioners for the appointment of a Whole-time Temporary REGISTRAR (anæsthetics) at the above Hospital. Appointment to commence as soon as possible for approximately 6-month period. Salary at rate of £775–£890 p.a., less £130 p.a. residential emoluments.

Applications, giving fullest details, together with copies of recent testimonials or the names of referees, to the Hospital Secretary.

BISHOP'S STORTFORD, HERTS. HAYMEADS HOSPITAL. (400 occupied beds. Midway between London and Cambridge. Main Line Railway from Liverpool Street.) Applications are invited from registered medical practitioners for a RESIDENT HOUSE OFFICER (surgical), first or second post held. Salary £350–£400 p.a., less £100 p.a. for residential emoluments. Appointment to commence as soon as possible.

Applications, stating age, nationality, qualifications and experience, with copies of recent testimonials or the names of referees, should be sent, as soon as possible, to the Hospital Secretary.

BISHOP'S STORTFORD AND DISTRICT HOSPITAL, Rye-street, BISHOP'S STORTFORD, HERTS. (67 Beds—medical, surgical, and maternity. Midway between London and Cambridge. Main Line Railway from Liverpool Street.) Applications are invited from registered medical practitioners for a RESIDENT HOUSE OFFICER (first or second post held). Salary £350–£400 p.a., less £100 p.a. for residential emoluments Appointment to commence as soon as possible.

Applications, stating age, nationality, qualifications and experience, with copies of recent testimonials or the names of referees, should be sent to the Hospital Secretary, Haymeads Hospital, Bishop's Stortford, Herts.

BLACKPOOL. VICTORIA HOSPITAL. (347 Beds.)

(1) SENIOR HOUSE OFFICER (E.N.T. Department). Recognised for D.L.O. and F.R.C.S.

(2) HOUSE OFFICER (E.N.T. Department). Recognised for D.L.O.

This is a busy General Hospital with a large Outpatient Department, and the posts offer excellent opportunities for experience under Consultant staff.

Applications, with references, to the Hospital Secretary.

BLACKBURN AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (paediatrics) required to take up duty on or about 1st October, 1953. Recognised post for D.C.H. Residence at Park Lee Hospital, Blackburn, with such duties as required by Consultant Paediatrician at the Royal Infirmary, and Queen's Park Hospital, Blackburn, and Victoria Hospital, Accrington.

Apply to the Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn.

BOSTON. GENERAL HOSPITAL. Sheffield Regional HOSPITAL BOARD. Whole-time RESIDENT REGISTRAR (general surgery and E.N.T.) required with relief duties in the Casualty Department. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 10th August, 1953, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

BOVEY TRACEY (near), SOUTH DEVON. HAWKMOOR CHEST HOSPITAL. (214 Beds, including Thoracic Surgical Unit of 40 Beds, 16 being for non-tuberculous cases.) There will shortly be a vacancy for a JUNIOR HOSPITAL MEDICAL OFFICER.

Applications, stating age, qualifications and experience, with names of referees or copies of testimonials, to be addressed to the Medical Superintendent.

BRADFORD. ROYAL EYE AND EAR HOSPITAL. HOUSE SURGEON (ophthalmic), vacant 17th August. Hospital recognised for D.O.M.S. and F.R.C.S. Salary £350–£450 p.a., less £100 p.a. residential emoluments.

Applications, stating age, nationality, qualifications, and experience, with copy testimonials, to Secretary, Bradford Royal Infirmary.

BRADFORD. ROYAL EYE AND EAR HOSPITAL. HOUSE SURGEON (E.N.T.), vacant 10th September. Recognised for D.L.O. and F.R.C.S. Salary £350–£450 p.a., less £100 p.a. residential emoluments.

Applications, stating age, nationality, qualifications and experience, together with copy testimonials, to Secretary, Bradford Royal Infirmary.

BRADFORD. ST. LUKE'S HOSPITAL. Senior House OFFICER (anæsthetics), vacant 1st September. Salary £670 p.a., less £130 p.a. residential emoluments.

Applications, stating age, nationality, qualifications, and experience, with copy testimonials, to Secretary, Bradford Royal Infirmary.

BOURNEMOUTH. ROYAL VICTORIA HOSPITAL, Poole-road, WESTBOURNE (HANTS). (72 Beds.) BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of HOUSE SURGEON for E.N.T. and ophthalmic duties. In addition to duties at the above Hospital the successful candidate will be required to assist in the E.N.T. outpatient clinics at the Royal Victoria Hospital, Bournemouth, and at Poole General Hospital, Dorset.

Applications to the Deputy Hospital Secretary, Royal Victoria Hospital, Shelley-road, Bournemouth.

BOURNEMOUTH. ROYAL VICTORIA HOSPITAL, Shelley-road. (492 Beds.) BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the immediate appointment of ORTHOPÆDIC SENIOR HOUSE OFFICER (resident). The post is recognised for the F.R.C.S. examination and is tenable for 12 months.

Applications to the Deputy Hospital Secretary.

BOURNEMOUTH. ROYAL VICTORIA HOSPITAL, Shelley-road. (492 Beds.) BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the immediate appointment of CASUALTY SENIOR HOUSE OFFICER (non-resident). The post is recognised for the F.R.C.S. examination and is tenable for 12 months.

Applications to the Deputy Hospital Secretary.

BRAINTREE, ESSEX. BLACK NOTLEY HOSPITAL. (544 Beds.) Applications invited for post of HOUSE OFFICER (orthopædic surgery), first, second, or third post. Post tenable for 6 months and is recognised under F.R.C.S. regulations. Salary in accordance with the terms of service issued by the Ministry of Health, plus £50 p.a.

Applications, with copies of 3 testimonials, should be forwarded to the Group Secretary, Colchester Hospital Management Committee, 14, Pope's-lane, Colchester, Essex.

BRAINTREE, ESSEX. BLACK NOTLEY HOSPITAL. (544 Beds.) Applications invited for post of SENIOR HOUSE OFFICER for Surgical Tuberculosis Unit, comprising chiefly orthopædic tuberculosis, genito-urinary tuberculosis, and other non-pulmonary and combined lesions. Post tenable for 1 year. Salary in accordance with the terms of service issued by the Ministry of Health.

Applications, with copies of 3 testimonials, should be forwarded to the Group Secretary, Colchester Hospital Management Committee, 14, Pope's-lane, Colchester, Essex.

BRAINTREE. BLACK NOTLEY HOSPITAL, and ESSEX COUNTY HOSPITAL, COLCHESTER. Applications invited for post of HOUSE SURGEON. First, second, or third post; tenable for 6 months. Duties to include work in general surgical and gynæcological wards. Salary in accordance with the terms of service issued by the Ministry of Health, plus £50 p.a. Recognised under F.R.C.S. regulations.

Applications, with copies of 3 testimonials, should be forwarded to the Group Secretary, Colchester Hospital Management Committee, 14, Pope's-lane, Colchester, Essex.

BRAINTREE, ESSEX. BLACK NOTLEY HOSPITAL. (544 Beds.) Locum SENIOR HOUSE OFFICER required for Surgical Tuberculosis Unit, comprising chiefly orthopædic tuberculosis, genito-urinary tuberculosis, and other non-pulmonary and combined lesions. Salary in accordance with the terms of service issued by the Ministry of Health.

Applications, with copies of 3 testimonials, should be forwarded to the Group Secretary, Colchester Hospital Management Committee, 14, Pope's-lane, Colchester, Essex.

BRIGHTON GENERAL HOSPITAL, Elm-grove, BRIGHTON, 7. Applications are invited for the appointment of a HOUSE SURGEON to the General Surgical Unit (60 Beds). Recognised for F.R.C.S. Vacant 18th August, 1953. Salary in accordance with national scale. The post is recognised as a pre-registration appointment.

Applications, stating age, qualifications, experience, naming 2 referees, to the Physician-Superintendent.

BRIGHTON, 1. ROYAL ALEXANDRA HOSPITAL FOR SICK CHILDREN, Dyke-road. (128 Beds.) SENIOR HOUSE OFFICER, £670 p.a., less £150 residential emoluments. Candidates should have experience in pædiatrics and be qualified to deal with surgical emergencies. The post is recognised for D.C.H.

Applications, stating age, nationality, experience, with copies of 3 testimonials, should reach the Administrative Officer not later than 10th August, 1953.

BRIGHTON. ROYAL SUSSEX COUNTY HOSPITAL. (300 Beds.) RESIDENT ANÆSTHETIST (Senior House Officer grade) required at the above Hospital, vacant now. Recognised for D.A.

Applications, stating age, qualifications and experience with names and addresses of 2 referees, to the Administrative Officer.

BRECHIN, ANGUS. STRACATHRO HOSPITAL. (680 Beds.) Applications are invited for the pre-registration appointment of HOUSE SURGEON (E.N.T. and gynæcology), which will shortly become vacant.

Applications, stating age and experience, and accompanied by 2 testimonials or names of 2 referees, should be addressed to the Medical Superintendent at the above address.

BRECHIN, ANGUS. STRACATHRO HOSPITAL. (680 Beds.) Applications are invited for the pre-registration appointment of HOUSE SURGEON (orthopædics), which will shortly become vacant.

Applications, stating age and experience, and accompanied by 2 testimonials or names of 2 referees, should be addressed to the Medical Superintendent at the above address.

BRECHIN, ANGUS. STRACATHRO HOSPITAL. (680 Beds.) Applications are invited for the pre-registration appointments of HOUSE SURGEONS (2) which will shortly become vacant.

Applications, stating age and experience, and accompanied by 2 testimonials or naming 2 referees, should be addressed to the Medical Superintendent at the above address.

BRISTOL. COSSHAM/FRENCHAY HOSPITAL MAN-AGEMENT COMMITTEE. FRENCHAY HOSPITAL. (499 staffed beds, expanding.) Applications are invited for the post of SENIOR HOUSE OFFICER in the Regional Neurosurgery Department. This post offers useful surgical experience and the opportunity of gaining a working knowledge of neurological diagnosis.

Applications to the Secretary, Frenchay Hospital, quoting "N.S.F." Names of 2 referees required.

BRISTOL MENTAL HOSPITALS (Barrow and Fish-PONDS). Applications are invited from registered medical practitioners for the appointment of SENIOR HOUSE OFFICER. Experience in general medicine or in neurology is an advantage. The Hospital Group includes modern admission-units, Neurosis Centre, and day hospital, with Departments of Applied Psychology, Electro-encephalography, and Biochemical Research. The appointment offers opportunities for experience in many aspects of acute and chronic psychiatric illness.

Applications, giving details of experience, and the names and addresses of 3 referees, should be made to the Medical Superintendent, Barrow Hospital, Barrow Gurney, near Bristol, not later than 2 weeks after the appearance of this advertisement.

BROMSGROVE. BARNSLEY HALL HOSPITAL. (750 Beds—mental and nervous diseases.) JUNIOR HOSPITAL MEDICAL OFFICER. Post offers experience in all branches of psychiatry.

Applications, with the names of 3 referees, to the Medical Superintendent.

CAMBRIDGE. PAPWORTH HOSPITAL. East Anglian REGIONAL HOSPITAL BOARD. MEDICAL REGISTRAR at above Hospital. Post provides wide range of experience in tuberculosis and includes duties in the Thoracic Surgical Unit. Appointment for 1 year, renewable for second year.

Applications, stating age, qualifications, and details of present and previous appointments, with names of 3 referees, to Secretary of Board, 117, Chesterton-road, Cambridge, by 10th August, 1953. Candidates invited to visit Hospital by arrangement with Hospital Management Committee Secretary at the Hospital.

CARDIFF. ST. DAVID'S HOSPITAL. (656 Beds.) Cardiff HOSPITAL MANAGEMENT COMMITTEE. RESIDENT SENIOR HOUSE OFFICER required from 1st August, 1953, in acute medical wards, working under direction of Consultants.

Form of application from Group Secretary, Cardiff Hospital Management Committee, 44, Cathedral-road, Cardiff.

CARDIFF ISOLATION HOSPITAL. Senior House OFFICER (resident) required at above Hospital.

Apply immediately to Group Secretary, Cardiff Hospital Management Committee, 44, Cathedral-road, Cardiff, giving particulars of age, qualifications, experience, &c., and names and addresses of 2 referees.

CARSHALTON, SURREY. ST. HELIER HOSPITAL. Applications are invited from registered medical practitioners for the following posts:—

(*a*) HOUSE SURGEON (general surgery with E.N.T. duties).
(*b*) HOUSE SURGEON (general surgery with duties in genito-urinary).

Both posts vacant end August and tenable for 6 months. Salary in accordance with National Health Service scale.

Applications, stating age, qualifications, &c., and the names and addresses of 2 referees, to be sent to the Group Secretary, St. Helier Hospital, Carshalton, Surrey.

CARSHALTON, SURREY. ST. HELIER HOSPITAL, Wrythe-lane. ST. HELIER GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for 2 posts of CASUALTY OFFICER (Senior House Officer), vacant August. Salary £670 p.a.

Applications, stating age, qualifications, and experience, with copies of 2 testimonials and the names of 2 referees, should be sent as soon as possible to the Group Secretary at the above address.

CHELMSFORD AND ESSEX HOSPITAL, London-road, CHELMSFORD. (160 Beds.) Applications are invited for the post of HOUSE PHYSICIAN (pre-registration post), to work in the general medical wards of the above Hospital. Duties will commence as soon as possible.

Applications, with copies of 3 recent testimonials, should be sent to the Secretary, Chelmsford Group Hospital Management Committee, London-road, Chelmsford.

CHELMSFORD AND ESSEX HOSPITAL. Applications are invited for the post of CASUALTY OFFICER (Senior House Officer), resident and tenable for 1 year. It offers excellent experience in the treatment of fractures and diagnosis of acute medical and surgical emergencies. Opportunity is given for the Casualty Officer to follow up his cases in the wards and to obtain operating experience in major theatre under the guidance of the Consultants or the Resident Surgical Officer. Off-duty time is generous and the post is one likely to suit both an Officer seeking a higher qualification in surgery or one intending General Practice. The vacancy will occur in September. Salary £670 p.a., with £130 deduction for residential emoluments.

Apply Secretary, Chelmsford Group Hospital Management Committee, Chelmsford and Essex Hospital, London-road, Chelmsford, Essex.

CHELMSFORD HOSPITAL MANAGEMENT COM-MITTEE. Full-time Locum Tenens SURGICAL REGISTRAR required for 3 weeks from 15th August to 6th September inclusive. Resident. The permanent post will be vacant from 1st October and will be advertised in due course. Preference will be given to holder of F.R.C.S.

Applications to the Secretary, Hospital Management Committee—Chelmsford Group, London-road, Chelmsford.

CHESTERFIELD ROYAL HOSPITAL. Senior House PHYSICIAN (Senior House Officer) required 1st August. National salary and conditions.

Please apply to— M. H. BOONE, Secretary,
Chesterfield Hospital Management Committee.

CHERTSEY, SURREY. ST. PETER'S HOSPITAL (late Botleys Park War Hospital). (430 Beds.) Required, SENIOR HOUSE OFFICER (Orthopædic Department). Previous orthopædic experience not essential. Appointment very suitable for candidate reading for a higher qualification, and is recognised by the Royal College of Surgeons for the F.R.C.S. Salary in accordance with terms and conditions of National Health Service. Post vacant 24th August.

Applications quoting reference (LAN), together with names and addresses of referees, to Physician-Superintendent, as soon as possible.

CHERTSEY, SURREY. ST. PETER'S HOSPITAL. (430 Beds.) The post of SENIOR HOUSE OFFICER in the Gynæcological and E.N.T. Departments will become vacant on 18th August.

Applications, together with testimonials, or names of referees, should be sent to the Physician-Superintendent as soon as possible.

COLCHESTER. ESSEX COUNTY HOSPITAL. (189 Beds.) Applications invited for post of SENIOR HOUSE OFFICER to Casualty and E.N.T. Departments at the above Hospital. Post tenable from mid-August for 6 months or 1 year. Salary in accordance with the terms of service issued by the Ministry of Health.

Applications, with copies of 3 testimonials, should be forwarded to the Group Secretary, Colchester Hospital Management Committee, 14, Pope's-lane, Colchester, Essex.

COLCHESTER. ESSEX COUNTY HOSPITAL. (189 Beds.) Applications invited for post of HOUSE OFFICER to Casualty and Radiotherapy Departments at above Hospital. First, second, or third post; tenable for 6 months. Salary in accordance with the terms of service issued by the Ministry of Health.

Applications, with copies of 3 testimonials, should be forwarded to the Group Secretary, Colchester Hospital Management Committee, 14, Pope's-lane, Colchester, Essex.

COLCHESTER GROUP HOSPITAL MANAGEMENT COMMITTEE. ESSEX COUNTY HOSPITAL, COLCHESTER (21 gynæcological beds); COLCHESTER MATERNITY HOSPITAL (22 obstetric beds). HOUSE OFFICER (Male or Female), obstetric and gynæcological. First, second, third, or pre-registration post; tenable for 6 months. Salary in accordance with the terms of service issued by the Ministry of Health.

Applications, with copies of 3 testimonials, should be forwarded to the Group Secretary, 14, Pope's-lane, Colchester, Essex.

COVENTRY AND WARWICKSHIRE HOSPITAL. (346 Beds.) RESIDENT SENIOR HOUSE OFFICER in Anæsthetics required, now vacant. Salary £670 p.a. Hospital recognised for D.A. Excellent experience in all types of general anæsthesia.

Applications to the Secretary, Group 20 Hospital Management Committee, Coventry and Warwickshire Hospital, Coventry.

COVENTRY. GULSON HOSPITAL. (329 Beds.) House PHYSICIAN required for 3rd September (106 general medicine beds).

Applications to the Secretary, Group 20 Hospital Management Committee, Coventry and Warwickshire Hospital, Coventry.

COTTINGHAM, E. YORKS. Senior House Officer for Raywell Sanatorium (48 Beds) and HOUSE OFFICER for Castle Hill Sanatorium (221 Beds) to work under supervision of Consultant Chest Physician. Sanatoria part of Group with major thoracic surgery and mass-radiography units and laboratory facilities.

Application forms from Group Secretary, Hull B Hospital Management Committee, De la Pole Hospital, Willerby, E. Yorkshire.

DUDLEY, STOURBRIDGE AND DISTRICT HOSPITAL GROUP. BIRMINGHAM REGION. Applications invited from registered practitioners for following appointments:—

The Guest Hospital, Dudley (154 Beds)

SENIOR HOUSE OFFICER (resident), surgical. Post now vacant. Salary £670 p.a., less £150 p.a. in respect of residential emoluments.

Corbett Hospital, Stourbridge (106 Beds)

SENIOR HOUSE OFFICER (resident), casualty. Post now vacant. Salary £670 p.a., less £150 p.a. in respect of residential emoluments.

SENIOR HOUSE OFFICER (resident), surgical, or HOUSE OFFICER (resident), surgical, pre-registration appointment. Post now vacant. Salary at appropriate rate less deduction for residential emoluments.

Wordsley Hospital, near Stourbridge (478 Beds)

SENIOR HOUSE OFFICER (resident), surgical. Post now vacant. Salary £670 p.a., less £150 p.a. in respect of residential emoluments.

SENIOR HOUSE OFFICER (Resident Anæsthetist). Post now vacant. Salary £670 p.a., less £150 p.a. in respect of residential emoluments. In addition to general surgery, experience is available in Orthopædics, Gynæcological and Plastic Units.

HOUSE OFFICER (resident), surgical, pre-registration appointment. Post now vacant. Salary at appropriate rate, less deduction of £100 p.a. in respect of residential emoluments.

Applications, stating age, experience, with copies of 3 recent testimonials, to— H. RAYMOND HURST,
Secretary, to the Management Committee.

The Guest Hospital, Dudley.

DOVER. ROYAL VICTORIA HOSPITAL. Applications are invited for the post of HOUSE SURGEON at the above Hospital. The post is recognised by the Royal College of Surgeons. Salary £350, £400, or £450 a year according to experience. A deduction of £100 a year will be made for residential emoluments.

Applications, stating age, qualifications, and the names and addresses of 2 referees, to the Group Secretary, "Ash-Eton," Radnor Park West, Folkestone.

DOVERCOURT, ESSEX. HARWICH AND DISTRICT HOSPITAL. (30 Beds.) Full-time Temporary SURGICAL REGISTRAR required immediately for 3 months. Salary in accordance with the terms of service issued by the Ministry of Health.

Applications, with copies of 3 testimonials, should be forwarded to the Secretary, Colchester Group Hospital Management Committee, 14, Pope's-lane, Colchester, Essex.

DONCASTER ROYAL INFIRMARY. (Post recognised for D.A.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT REGISTRAR (anæsthetics) required. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 10th August, 1953, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

DONCASTER ROYAL INFIRMARY. (Recognised under the regulations for the Fellowship and D.L.O.) DONCASTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the whole-time post of SENIOR HOUSE OFFICER (E.N.T. Department), in accordance with the terms and conditions of service for hospital medical and dental staffs (England and Wales). Salary at the rate of £670 p.a., less £130 p.a. for board, residence, &c.

Applications, stating age, education, qualifications, and details of present and previous appointments with dates, together with copies of 3 testimonials, should be forwarded to—
ARTHUR JONES, Group Secretary.

Doncaster Royal Infirmary.

DONCASTER ROYAL INFIRMARY. (Recognised under the regulations for the F.R.C.S.) DONCASTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of SECOND CASUALTY OFFICER (Senior House Officer) at above Infirmary. Salary £670 p.a., from which a deduction at the rate of £130 p.a. will be made for residential emoluments.

Applications, stating age, qualifications, and details of present and previous appointments with dates, and enclosing copies of 3 recent testimonials, should be forwarded to—
ARTHUR JONES, Secretary to the Committee.

Doncaster Royal Infirmary.

DUNFERMLINE MATERNITY HOSPITAL. (56 Beds.) 2 OBSTETRICAL HOUSE SURGEONS (resident) required at the above Hospital. The Hospital is recognised for the D.Obst.R.C.O.G. The successful applicants will be required to take up duty (1) in mid-September, 1953, and (2) at the beginning of October, 1953.

Applications, giving age, nationality, qualifications and experience, with copies of 3 testimonials, should be sent to the Medical Superintendent, Maternity Hospital, St. Leonards, Dunfermline.

DARLINGTON MEMORIAL HOSPITAL. Applications are invited from Male or Female practitioners with experience for the post of SURGICAL REGISTRAR (Senior House Officer) which is one of a surgical team of 2 Registrars and 1 House Officer responsible for surgical beds and casualty. The post is recognised for the F.R.C.S.(Eng.) Salary £670 p.a., deduction of £150 p.a. for full residential emoluments. The post is tenable for 12 months and is renewable annually.

Apply with references, stating age and experience, to—
G. W. BECKWITH, Group Secretary.

DARLINGTON MEMORIAL HOSPITAL. (210 Beds.) DARLINGTON DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of HOUSE SURGEON (resident), which post is recognised for the F.R.C.S. (Eng.). Salary in accordance with national scale.

Apply, giving age and references, to the undersigned forthwith. G. W. BECKWITH, Group Secretary.

DARTFORD HOSPITAL MANAGEMENT COMMITTEE.

SENIOR HOUSE OFFICER (anæsthetics) at Joyce Green Hospital, Dartford.

*HOUSE SURGEON (general) at the Joyce Green Hospital, Dartford.

HOUSE SURGEON (orthopædics) at the Southern Hospital, Dartford.

*HOUSE OFFICER (general medicine) at the Southern Hospital, Dartford.

HOUSE OFFICER (E.N.T. and ophthalmology) at the Southern Hospital, Dartford.

*Appointment approved for pre-registration purposes.

Applications, stating age, qualifications, experience, nationality, and the names of 2 persons to whom reference may be made, to be sent, for House Officers, to the Medical Superintendent of the hospital concerned, and, for Senior House Officer, to the Group Secretary, Dartford Hospital Management Committee, the Bow Arrow Hospital, Dartford.

DERBY. CITY HOSPITAL. (Post recognised for D.A.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT REGISTRAR (anæsthetics) required. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 10th August, 1953, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

DEWSBURY. STAINCLIFFE GENERAL HOSPITAL. (314 Beds.) RESIDENT SURGICAL OFFICER (Senior House Officer grade). Post now vacant. The Surgical Unit comprises 66 Beds and the Hospital is recognised for the F.R.C.S.

Applications, giving full details to the Administrative Officer at the Hospital.

DEWSBURY. STAINCLIFFE GENERAL HOSPITAL. (314 Beds.) HOUSE OFFICER (general medicine and dermatology), first, second, or third post, vacant now and tenable for 6 months. Recognised pre-registration appointment.

Applications, with full particulars, to the Administrative Officer at the Hospital.

DEWSBURY. STAINCLIFFE GENERAL HOSPITAL. (314 Beds.) A vacancy for a RESIDENT MEDICAL OFFICER (Junior Hospital Medical Officer grade) will arise shortly. The Hospital has a Medical Unit of 68 adult beds and 34 beds for children. The Resident Medical Officer has 2 resident House Physicians to assist him.

Application, giving full details of experience, &c., should be addressed to the Group Secretary at 20, Oxford-road, Dewsbury.

DEWSBURY. STAINCLIFFE GENERAL HOSPITAL. (314 Beds.) HOUSE OFFICER (general surgery), first, second, or third post, vacant now and tenable for 6 months. Recognised pre-registration appointment. The Hospital is recognised for the F.R.C.S.

Applications, with full particulars, to the Administrative Officer at the Hospital.

DORKING GENERAL HOSPITAL, Horsham-road, DORKING, SURREY. (252 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER (surgical) for immediate appointment or as Locum Tenens if preferred.

Apply to the Medical Superintendent.

EAST CUMBERLAND HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the following HOUSE OFFICER appointments which are now vacant :—

Cumberland Infirmary, Carlisle (340 Beds)

1—General Surgery.
1—General Medicine.
1—Orthopædics.
1—" Specials "—(E.N.T. and Eyes).

Applications, with names of 2 referees, should be forwarded immediately to the Secretary, East Cumberland Hospital Management Committee, Cumberland Infirmary, Carlisle.

ENFIELD, MIDDLESEX. CHASE FARM HOSPITAL. ENFIELD GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of RESIDENT HOUSE SURGEON (second or third post), vacant shortly for duties with a General Surgical Unit, doing some orthopædic work. Post recognised by the Royal College of Surgeons. 6 months appointment.

Applications, stating age, qualifications, experience, and nationality, with the names of 2 referees, to the Secretary, Enfield Group Hospital Management Committee immediately.

ENFIELD, MIDDLESEX. CHASE FARM HOSPITAL. ENFIELD GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of RESIDENT HOUSE SURGEON (first post), vacant 18th August. General surgical duties. R practitioners within 3 months of qualification eligible. 6 months appointment.

Applications, stating age, qualifications, experience, and nationality, with the names of 2 referees, to the Secretary of the Management Committee, by 7th August, 1953.

EPSOM, SURREY. ST. EBBA'S HOSPITAL. South WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of REGISTRAR at above Hospital. The Hospital is principally concerned with the treatment of voluntary cases of good prognosis, has a high turnover of cases, uses all modern treatment methods, and has teaching linkages with 2 London training hospitals. There are outpatient departments and a special unit for juvenile psychiatric cases. Salary, &c., in accordance with the agreed terms and conditions of service of hospital medical and dental staffs. For residents a charge of £3 3s. a week is made for full residential amenities. Candidates may visit the Hospital by appointment with the Physician-Superintendent.

Application forms may be obtained from the Group Secretary, St. Ebba's and Belmont Group Hospital Management Committee, Group Office, Belmont Hospital, Brighton-road, Sutton, Surrey, and completed forms (5 copies) should be returned to him within 2 weeks of the appearance of this advertisement.

EPPING. ST. MARGARET'S HOSPITAL. (485 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER (pathology) becoming vacant 1st August, 1953. Salary on national scale, less deduction for board, lodging, &c. Busy department in large general hospital, with easy access to London. Some experience in pathological department desirable.

Applications, with copies of 2 recent testimonials, to reach the Group Secretary, Epping Group Hospital Management Committee, St. Margaret's Hospital, Epping, Essex, by 17th August, 1953.

FOLKESTONE. ROYAL VICTORIA HOSPITAL. Applications are invited for the post of HOUSE SURGEON. The duties will be mainly obstetrical and gynæcological with some general surgery. Salary £350, £400, or £450 a year according to experience. A deduction of £100 a year will be made for residential emoluments.

Applications, stating age, qualifications, and the names and addresses of 2 referees, to the Group Secretary, " Ash-Eton," Radnor Park West, Folkestone.

FAREHAM, HANTS. KNOWLE HOSPITAL. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER at the above Mental Hospital, where all forms of modern psychiatric treatment are undertaken. Terms and conditions of service as approved for hospital medical and dental staffs, employed in the National Health Service. Salary £700–£50–£1000 p.a. Single residential accommodation is available, but Officers who so desire may live outside the Hospital.

Applications should be sent without delay to the Physician-Superintendent. M. WALSH, Group Secretary,
Knowle Hospital Management Committee.

EXETER. ROYAL DEVON AND EXETER HOSPITAL. EXETER AND MID-DEVON HOSPITALS MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners (Male and Female) for the post of HOUSE SURGEON, vacant 3rd August, 1953. The appointment is for a period of 6 months. The post is also open to provisionally registered practitioners.

Applications, with copies of 2 recent testimonials, to be forwarded to the Hospital Secretary.

EXETER. ROYAL DEVON AND EXETER HOSPITAL. (Bed Complement—320. Staff—2 Senior Registrars, 5 Senior House Officers, 7 Junior House Officers.) EXETER AND MID-DEVON HOSPITALS MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the appointment of SENIOR HOUSE OFFICER (anæsthetic), resident or non-resident, vacant now. Preference will be given to candidates studying for the D.A. for which the Hospital is recognised. The duties entail some night emergency work, and the successful candidate must be on the telephone and reside within the City boundaries. Assistance in obtaining accommodation will be given.

Applications, with copies of 2 recent testimonials, to the Hospital Secretary immediately.

GOODMAYES HOSPITAL, Goodmayes, Ilford, Essex. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER. The Hospital is situated within reasonable travelling distance from the centre of London. Candidates should have some psychiatric experience. The Hospital services provide a Unit for the treatment of psychoneurosis, and there are Departments of Electro-encephalography and Clinical Psychology. Outpatient facilities include psychiatric clinics at General Hospitals, a Child Guidance Clinic, and Social Therapy Clubs. The salary is in accordance with the national scale, commencing at £700 p.a., rising to £1000. There is residential accommodation for which a charge of £150 p.a. is made.

Applications, with names of 3 referees, should be forwarded to the Physician-Superintendent as soon as possible.

GRIMSBY GENERAL HOSPITAL. (220 Beds.) Grimsby HOSPITALS MANAGEMENT COMMITTEE. HOUSE OFFICER (surgical and E.N.T.). Pre-registration post (recognised for the D.L.O.) under the Medical Act, 1950, vacant 5th September, 1953. Salary and conditions of service in accordance with national scale.

Applications, with names of 2 referees, to Hospital Secretary, Grimsby General Hospital.

GRIMSBY GENERAL HOSPITAL. (220 Beds.) Grimsby HOSPITALS MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER (gynæcological), Male or Female, for duties at the above-named Hospital and Scartho Road Infirmary, Grimsby. The post is vacant as from 5th August, 1953.

Applications, with names of 2 referees, to Hospital Secretary, Grimsby General Hospital.

GRIMSBY MATERNITY HOSPITAL. (45 Beds.) Applications are invited for the post of SENIOR OBSTETRIC HOUSE OFFICER (resident), vacant on 31st August, 1953. A large proportion of abnormal cases are treated.

Apply immediately, with names of 2 referees, to the Secretary, Grimsby Hospital Management Committee, 3, Queen's-parade, Grimsby.

GUILDFORD GROUP HOSPITAL MANAGEMENT COMMITTEE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for the post of REGISTRAR to the Orthopædic and Traumatic Unit serving the Group. The appointment is for 1 year in first instance and may be renewed for a further year ; it is non-resident and the candidate appointed will be required to live within a short distance of Royal Surrey County Hospital. The unit comprises 50 short-term orthopædic and traumatic beds. Preference will be given to applicants with a higher qualification. Candidates may visit the Hospital by arrangement.

Application forms from Group Secretary, Guildford Group Hospital Management Committee, St. Luke's Hospital, Guildford, which should be returned to him to arrive not later than 14th August, 1953.

HAVERFORDWEST. PEMBROKE COUNTY WAR MEMORIAL HOSPITAL. (151 Beds—Recognised for Pre-registration Service.) Applications are invited for the post of RESIDENT HOUSE OFFICER (surgical). Salary £350, £400, or £450 p.a., according to experience, plus grant of £50 p.a., less £100 p.a. for board-residence.

Applications, stating age, qualifications, experience, and nationality, with names and addresses of 3 referees, to Group Secretary, West Wales Hospital Management Committee, Glangwili, Carmarthen.

HASTINGS. ROYAL EAST SUSSEX HOSPITAL. (150 Beds.) HOUSE SURGEON required (resident), Male or Female. Pre-registration post now vacant. National scale of salary.

Apply to Hospital Administrator.

HASTINGS. ROYAL EAST SUSSEX HOSPITAL. (150 Beds.) SENIOR HOUSE OFFICER (casualty and orthopædic), post vacant now. National scale of salary.

Apply to Hospital Administrator.

HALIFAX GENERAL HOSPITAL. (425 Beds.) House SURGEON required at the above acute General Hospital.

Applications to Group Secretary, Royal Halifax Infirmary, Halifax.

HEMEL HEMPSTEAD, HERTS. WEST HERTS HOS-PITAL. (170 Beds—5 Residents.) Applications are invited for the post of HOUSE SURGEON (first or subsequent post) for a term of 6 months.

Applications, with full details and copies of 2 recent testimonials, should be sent to the Administrator.

HERTFORD COUNTY HOSPITAL. (171 Beds. Hospital situated 21 miles from London.) Applications are invited for the appointment of HOUSE SURGEON (Male or Female), first or second post held, for general surgery, gynæcology, and obstetrics. Pre-registration post. 6 months appointment. Salary at rate of £350 or £400 p.a. respectively, less £100 p.a. residential emoluments. Duties to commence 1st August, 1953.

Applications to the Group Secretary, Hertford Group Hospital Management Committee, Hertford County Hospital, Hertford, Herts.

HERTFORD COUNTY HOSPITAL. (171 Beds. Hospital situated 21 miles from London.) CASUALTY HOUSE OFFICER (Male or Female), second or third post held, with attachment to Pædiatrician and Ophthalmic Consultant. Salary £400–£450 p.a., less £100 p.a. residential emoluments. Appointment to commence mid-August. Applications for locum period would be considered.

Apply, with full details and references, to Secretary, Hertford County Hospital, Hertford, Herts.

HEREFORD. GENERAL HOSPITAL. (154 Beds.) HOUSE OFFICER (pædiatrics) required immediately.

Applications, with copies of 2 recent testimonials, to the Secretary, Hospital Management Committee, County Hospital, Hereford.

HEREFORD. GENERAL HOSPITAL. (154 Beds.) HOUSE OFFICER (medicine) required immediately.

Applications, with copies of 2 recent testimonials, to the Secretary, Hospital Management Committee, County Hospital, Hereford.

HEREFORD. COUNTY HOSPITAL. (333 Beds.) Applications are invited from registered medical practitioners for appointment of HOUSE OFFICER (general surgery).

Applications, with copies of 2 recent testimonials, should be sent to the Medical Superintendent, County Hospital, Hereford.

HILLINGDON HOSPITAL, near Uxbridge, Middlesex. HOUSE PHYSICIAN (resident) required. Recognised for M.D.(Lond.) Branch 1 and for pre-registration House Officers.

Applications, stating age, nationality, qualifications and experience, together with copies of not more than 3 recent testimonials, to Medical Director by 10th August.

HITCHIN HOSPITALS, Hitchin, Herts. Applications are invited for the post of RESIDENT HOUSE SURGEON at the North Herts Hospital. Vacant 2nd September.

Applications, stating age, nationality, qualifications, and experience, together with copies of 3 recent testimonials, to be sent to the Medical Director, Lister Hospital, Hitchin, Herts.

HUDDERSFIELD HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of HOUSE SURGEON to the Princess Royal Maternity Home (57 Beds) to commence on 16th August, 1953. The holder of the post, which is recognised for the D.Obst. R.C.O.G., will have access to the abnormal maternity and gynæcological beds at the Royal Infirmary. The Department is under the control of 2 Consultant Obstetricians and Gynæcologists. Salary in accordance with the terms and conditions for hospital medical and dental staffs. The post is recognised as a pre-registration appointment.

Applications to be addressed to—

H. J. JOHNSON,
Secretary to the Management Committee.
Royal Infirmary, Huddersfield.

HUDDERSFIELD ROYAL INFIRMARY. (312 Beds.) HUDDERSFIELD HOSPITAL MANAGEMENT COMMITTEE. HOUSE PHYSICIAN required to commence duty on 21st August, 1953. Salary in accordance with the terms and conditions of service for hospital medical and dental staffs, with full residential emoluments. The post is recognised as a pre-registration appointment.

Applications, together with copies of 3 recent testimonials, to be addressed to the undersigned as soon as possible.

H. J. JOHNSON, Secretary to the Management Committee.
The Royal Infirmary, Huddersfield.

HUDDERSFIELD ROYAL INFIRMARY. (312 Beds.) HUDDERSFIELD HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON required to commence duty immediately. Salary in accordance with the terms and conditions of service for hospital medical and dental staffs, with full residential emoluments. The post is recognised as a pre-registration appointment.

Applications, together with copies of 3 recent testimonials, to be addressed to the undersigned as soon as possible.

H. J. JOHNSON, Secretary to the Management Committee.
The Royal Infirmary, Huddersfield.

HULL. VICTORIA HOSPITAL FOR SICK CHILDREN, Park-street. (143 Beds.) HULL A GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the following :—

HOUSE SURGEON—post now vacant.
HOUSE SURGEON—post vacant middle September.
HOUSE PHYSICIAN—post vacant middle September.

6-monthly term in each case. All count towards D.C.H. qualification. Salary as per Ministry of Health terms of service.

Replies, with testimonials, to be sent to the Hospital Secretary.

HULL. KINGSTON GENERAL HOSPITAL. (398 Beds.) Applications are invited for the appointments of 2 HOUSE OFFICERS ; 1 mainly gynæcology and 1 general surgery (recognised pre-registration appointments). Salary £350, £400, or £450 according to experience. The posts are resident and tenable for 6 months.

Applications, to be forwarded to the Secretary, Hull A Group Hospital Management Committee.

HULL ROYAL INFIRMARY. Hull A Group Hospital MANAGEMENT COMMITTEE. Applications are invited for the appointment of RESIDENT SURGICAL OFFICER (Senior House Officer grade), vacant now. Recognised for F.R.C.S. Salary will be at the rate of £670 p.a., less deduction of £130 p.a. for residential emoluments. National conditions of service. Appointment for 12 months in the first instance. Notice 2 months either side.

Application forms from the Hospital Secretary.

IPSWICH. EAST SUFFOLK AND IPSWICH HOSPITAL. (360 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER RESIDENT ANÆSTHETIST. The post, which is normally of 1 years duration, is recognised for the D.A. examination.

Applications, stating age, nationality, together with recent testimonials, to Hospital Secretary.

IPSWICH BOROUGH GENERAL HOSPITAL, Heath-road, IPSWICH. (275 Beds.) Applications are invited for the posts of HOUSE PHYSICIAN (pre-registration) to both the General Physician and the Pædiatric Department at this Hospital. Previous pædiatric experience is not required in the post involving these duties. The posts are of House Officer grade and are recognised for pre-registration purposes.

Applications, giving details of qualifications, age, nationality, &c., together with copies of 2 recent testimonials to the Hospital Secretary.

IPSWICH. ST. HELEN'S HOSPITAL. (100 Beds for infectious diseases, pulmonary tuberculosis, and long-stay orthopædics. The Area Chest Clinic is in the Hospital.) IPSWICH GROUP HOSPITAL MANAGEMENT COMMITTEE. HOUSE PHYSICIAN required. Salary £450 p.a. Accommodation available for married man. The person appointed will be required to undertake certain duties in the Children's Wards at the Borough General Hospital in addition to the duties at St. Helen's Hospital.

Applications, with full particulars, to JOHN WILLIAMS, Group Secretary, at East Suffolk and Ipswich Hospital, Ipswich.

ILKLEY (near). THE HOSPITAL, Middleton-in-Wharfe-DALE, near ILKLEY. (130 Beds.) MIDDLETON AND GRASSINGTON GROUP. Applications are invited for the appointment of JUNIOR HOSPITAL MEDICAL OFFICER (resident) at the above Hospital for tuberculosis. Experience in tuberculosis essential and some experience in obstetrics desirable. Remuneration £700 rising to £1000 p.a., in accordance with national award, from which will be made an appropriate deduction for full board-residence.

Applications to the Secretary at the above Hospital.

ISLEWORTH. WEST MIDDLESEX HOSPITAL. South WEST MIDDLESEX HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER required for Admissions and Casualty Department. Must have held medical and surgical posts.

Applications, stating age, nationality, qualifications, and experience, with copies of up to 3 recent testimonials, to Group Secretary, Management Committee, West Middlesex Hospital, Isleworth, Middlesex, by 11th August, 1953.

ILFORD, ESSEX. KING GEORGE HOSPITAL. There will be a vacancy for a HOUSE SURGEON (pre-registration) at the above Hospital on 15th August, 1953 (E.N.T. and general surgery). The post will be tenable for 6 months.

Applications, giving full particulars and accompanied by testimonials, should be sent to the undersigned within 7 days of the appearance of this advertisement.

G. AUSTIN HEPWORTH, Secretary,
Ilford and Barking Group Hospital Management Committee.
King George Hospital, Ilford.

KINGSTON HOSPITAL, Wolverton-avenue, Kingston-UPON-THAMES. KINGSTON GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from suitably qualified and experienced medical officers for the following posts which become vacant on 1st October, 1953. Both posts are recognised for the F.R.C.S.

SENIOR HOUSE OFFICER (general surgery).
SENIOR HOUSE OFFICER (orthopædic and casualty).

The appointments may be resident or on a Duty Room basis.

Applications, stating age, experience and qualifications, and accompanied by 2 recent testimonials or names of referees, should reach the Physician-Superintendent of the Hospital within 10 days of the appearance of this advertisement.

KETTERING GENERAL HOSPITAL. (171 Beds.) Applications are invited for the pre-registration post of HOUSE PHYSICIAN, vacant now. The appointment is for 6 months. There are 5 resident Officers and full Consultant staff.

Applications, stating age, nationality, qualifications, and enclosing copies of 2 testimonials, should be forwarded as soon as possible to the Group Secretary, General Hospital, Kettering.

LEICESTER ROYAL INFIRMARY. Sheffield Regional HOSPITAL BOARD. Whole-time RESIDENT REGISTRAR (anæsthetics) required. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 17th August, 1953, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

LLANELLY HOSPITAL. (164 Beds.) Glantawe Hospital MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the resident post of SENIOR HOUSE OFFICER for work in the Surgical Unit, and with duties in the Casualty Department of the above Hospital.

Full particulars stating age, qualifications and experience, should be addressed to the undersigned.

O. C. HOWELLS, Group Secretary,
Glantawe Hospital Management Committee.
St. Helen's-road, Swansea.

LIVERPOOL, 13. RATHBONE HOSPITAL, Mill-lane. Applications are invited for the post of SENIOR HOUSE OFFICER. The Hospital has 144 Beds and admits the usual infectious diseases. Facilities might be given to the applicant appointed to attend the D.P.H. or similar course at Liverpool University. Salary £670 p.a., less £130 p.a. in respect of residential emoluments.

Applications, on forms obtainable from the undersigned, to be returned completed within 10 days of this advertisement.

H. BLYTHE, Group Secretary.
Broadgreen Hospital, Liverpool, 14.

LIVERPOOL, 14. BROADGREEN HOSPITAL. Appli-cations are invited from registered medical practitioners for the post of SENIOR HOUSE OFFICER in the Regional Thoracic Surgical Centre. Salary £670 p.a., less £130 p.a. in respect of residential emoluments.

Applications, on forms obtainable from the undersigned at the above address, to be returned not later than 10 days after the appearance of this advertisement.

H. BLYTHE, Group Secretary.

LEAMINGTON SPA. WARNEFORD GENERAL HOSPITAL. (207 Beds.) SOUTH WARWICKSHIRE HOSPITAL GROUP (NO. 14). RESIDENT HOUSE SURGEON (general surgery). Post vacant 11th September, 1953. Recognised for pre-registration.

Apply to the Hospital Secretary.

LEAMINGTON SPA. WARNEFORD GENERAL HOSPITAL. (207 Beds.) SOUTH WARWICKSHIRE HOSPITAL GROUP (NO. 14). Applications are invited for the appointment of HOUSE PHYSICIAN. Post vacant on 2nd September, 1953. Pre-registration post.

Applications, with 2 recent testimonials, should be sent to the Hospital Secretary as soon as possible.

LEAMINGTON SPA. WARNEFORD GENERAL HOSPITAL. (207 Beds.) SOUTH WARWICKSHIRE HOSPITAL GROUP (NO. 14). HOUSE SURGEON (obstetrics and gynæcology). Recognised for D.Obst.R.C.O.G.

Apply as soon as possible to the Hospital Secretary.

LEEDS REGIONAL HOSPITAL BOARD invites applications for the post of REGISTRAR in General Surgery for duties at the Harrogate and District General Hospital (resident).

Applications, stating age, qualifications, and details of present and previous appointments with dates, together with the names of 3 referees, should be forwarded to the Secretary, Joint Registrars Committee, Park-parade, Harrogate, not later than 7th August, 1953.

LEEDS REGIONAL HOSPITAL BOARD invites applications for the following REGISTRAR posts :—

Chest Diseases

Castle Hill Sanatorium, Cottingham, East Yorks. (non-resident).

General Surgery

(*a*) Keighley and District Victoria Hospital, Keighley (resident/non-resident).

(*b*) Dewsbury, Batley and Mirfield Group (resident).

(*c*) Halifax General Hospital (resident).

Infectious Diseases

Leeds Road Hospital, Bradford (resident).

Orthopædic Surgery

(*a*) York A and Tadcaster Group (non-resident) for duties mainly at York General and City Hospitals.

(*b*) Huddersfield Royal Infirmary and other hospitals in the Huddersfield Group (non-resident).

Pathology

Halifax Group Hospital Management Committee (non-resident).

Psychiatry

(*a*) Storthes Hall Hospital, Kirkburton, near Huddersfield, and associated clinics. The post will be resident and a flat is available. Facilities for attendance at the Leeds University will be provided if the successful candidate is studying for the D.P.M.

(*b*) Scalebor Park Hospital (300 Beds—annual admission-rate 350–400). Residential accommodation for a single person; a house may be available. Facilities for attendance at the Leeds University will be provided if the successful candidate is studying for the D.P.M.

Applications, stating age, qualifications and details of present and previous appointments with dates, together with the names of 3 referees, should be forwarded to the Secretary, Joint Registrars Committee, Park-parade, Harrogate, not later than 7th August, 1953.

LEEDS REGIONAL HOSPITAL BOARD. Short-term LOCUM TENENS appointments in the Registrar grade are constantly available at hospitals in the area of the Board, particularly in the specialties of General Medicine, General Surgery and Psychiatry.

Suitably experienced practitioners interested in such appointments are invited to communicate with the Secretary, Joint Registrars Committee, Park-parade, Harrogate.

LEEDS, 9. ST. JAMES'S HOSPITAL. Leeds A Group HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners (Male and Female) for the appointment of SENIOR HOUSE OFFICER (psychiatry). The department consists of emergency admission wards and units for the treatment of early psychotic and neurotic cases. There is a large outpatient commitment. Facilities will be provided for attendance at Leeds University if the successful applicant is studying for the D.P.M. The appointment will be for a period of 1 year and the salary will be in accordance with the agreed terms and conditions of service of hospital medical and dental staffs—namely, £670 p.a., with an appropriate deduction in respect of board, lodging, and other services provided.

Applications, stating age, qualifications, experience, &c., together with the names of 2 referees, to be forwarded to the undersigned as soon as possible.

J. FOLKARD, Secretary to the Committee.

Administrative Offices, St. James's Hospital, Leeds, 9.

LYMINGTON HOSPITAL, Lymington, Hants. (107 Beds.) SENIOR HOUSE OFFICER (surgical) required immediately. Post normally tenable 1 year.

Apply, stating qualifications and experience, with copies of recent testimonials, to the Group Secretary, Southampton Hospital Management Committee, Bullar-street, Southampton.

LYMINGTON HOSPITAL, Lymington, Hants. (107 Beds.) RESIDENT SENIOR HOUSE OFFICER (medical) required from mid-September.

Applications, with copies of testimonials, to be submitted as soon as possible to the Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

MARGATE. GENERAL HOSPITAL. (132 Beds.) House SURGEON (approved pre-registration post). Salary at rate of £350–£450 p.a., according to experience, less £100 for residential emoluments.

Applications, with copies of testimonials, to Hospital Secretary.

LOUTH, LINCS. COUNTY INFIRMARY. (200 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER (surgical) or JUNIOR HOUSE OFFICER (pre-registration), at this busy General Hospital. The post is resident and appropriate deductions will be made in respect of board, residence, &c.

Applications, giving full particulars, together with names of 2 referees, to be addressed to the Hospital Secretary.

MALVERN, WORCS. ST. WULSTAN'S HOSPITAL. RESIDENT MEDICAL OFFICER (Junior Hospital Medical Officer) required. The post offers good experience in modern treatment of pulmonary tuberculosis and in all forms of major and minor surgery. Some experience necessary, either surgical or medical. National Health Service conditions of service.

Applications to the Physician-Superintendent.

MANSFIELD AND DISTRICT GENERAL HOSPITAL. (207 Beds.) MANSFIELD HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of HOUSE SURGEON (pre-registration or Senior House Officer post). Post recognised for F.R.C.S. examinations.

Applications, stating age and qualifications, together with copies of 2 recent testimonials, to be forwarded to Group Secretary, Mansfield Hospital Management Committee, Crow Hill-drive, Mansfield.

MANSFIELD AND DISTRICT GENERAL HOSPITAL. (207 Beds.) MANSFIELD HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER in Anæsthetics (resident). The post is recognised for the D.A. Appointment will be for 1 year. Salary £670 p.a., with a deduction of £135 in respect of residential emoluments.

Applications, stating age, qualifications and experience, together with copies of 2 testimonials, should be forwarded to the undersigned immediately.

A. ASHWORTH, Group Secretary,
Mansfield Hospital Management Committee.
Oak Bank, Crow Hill-drive, Mansfield.

MANSFIELD HOSPITAL MANAGEMENT COMMITTEE. KING'S MILL HOSPITAL, SUTTON-IN-ASHFIELD, AND VICTORIA HOSPITAL, MANSFIELD. Applications are invited for the post of RESIDENT SENIOR HOUSE OFFICER (Male or Female) in Obstetrics and Gynæcology for duties at the following :—

King's Mill Hospital—Gynæcological Unit (46 Beds) and Outpatient Services.

Victoria Hospital—Obstetrical Unit (32 Beds).

The duties of the post will be predominantly gynæcological. The successful candidate will reside at King's Mill Hospital. Salary will be at the rate of £670 p.a., less emoluments.

Applications, stating age, qualifications, experience, together with copies of recent testimonials or names of 2 referees, should be forwarded to A. ASHWORTH, Group Secretary,

Oak Bank, Crow Hill-drive, Mansfield, Notts.

MAIDSTONE. WEST KENT GENERAL HOSPITAL. (135 Beds.) MID-KENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of RECEIVING-ROOM OFFICER. Salary £670 a year, with deduction of £150 a year for residential emoluments.

Applications to the Administrative Officer at the Hospital as soon as possible.

MAIDSTONE. WEST KENT GENERAL HOSPITAL. (135 Beds.) MID-KENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of SENIOR HOUSE SURGEON. Post recognisable for the F.R.C.S.(Eng.). Salary £670 a year, with deduction of £150 a year for residential emoluments.

Applications to the Administrative Officer at the Hospital as soon as possible.

MAIDSTONE. KENT COUNTY OPHTHALMIC AND AURAL HOSPITAL. (113 Beds.) MID-KENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of SENIOR HOUSE OFFICER in the Ophthalmic Department of the above Hospital. The Hospital is recognised by the Examining Boards for the F.R.C.S. and the D.O. Appointment will be for 12 months. Salary £670 a year, less £150 a year for residential emoluments.

Applications, should be forwarded as soon as possible, to the Administrative Officer, Kent County Ophthalmic and Aural Hospital, Church-street, Maidstone.

MAIDSTONE. PRESTON HALL HOSPITAL, British LEGION VILLAGE, MAIDSTONE, KENT. Applications are invited for the appointment of SENIOR HOUSE OFFICER. Salary £670 p.a., national scale and conditions. The Sanatorium contains 330 Beds for the treatment of pulmonary tuberculosis. All modern forms of treatment are carried out, including major thoracic surgery.

Applications, stating age, qualifications, and names of 2 referees, to be sent by not later than 15th August, to—

A. A. HOWICK, Secretary to the Management Committee.

MANCHESTER, 9. BOOTH HALL CHILDREN'S HOSPITAL. RESIDENT SENIOR HOUSE OFFICER (surgical). Conditions are those of national scale.

Applications, stating age, nationality, and usual relevant particulars, and enclosing copies of 2 recent testimonials, should be sent to the Medical Superintendent as soon as possible.

MANCHESTER. BAGULEY HOSPITAL, Wythenshawe. SOUTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered practitioners preferably under 40 years of age for the resident post of JUNIOR HOSPITAL MEDICAL OFFICER at the above Hospital, which has 402 Beds for the treatment of pulmonary tuberculosis and is the major Thoracic Surgical Centre for the Region. Post will include duties at chest clinics.

Applications, stating age, nationality, qualifications, experience, and names of 3 referees, to be forwarded to the Group Secretary, Withington Hospital, Manchester, 20, within 7 days of the appearance of this advertisement.

MANCHESTER. WEST MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. PARK HOSPITAL, DAVYHULME. (General Hospital—426 Beds.)

1 SENIOR HOUSE OFFICER (general surgery). Post now vacant.

1 SENIOR HOUSE OFFICER (non-tuberculous thoracic surgery) for Manchester Regional Hospital Board Centre. Vacant mid-August, 1953.

1 HOUSE OFFICER (E.N.T. surgery). (Pre-registration.) Post now vacant.

General surgery posts recognised for F.R.C.S. examination.

Forms from Secretary.

MANCHESTER AND SALFORD HOSPITAL FOR SKIN DISEASES, Quay-street, MANCHESTER, 3. SALFORD HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER (resident), now vacant. The appointment is for a period of 12 months.

Applications, stating age, qualifications with dates, nationality, and accompanied by copies of 3 recent testimonials, to be sent to the Hospital Secretary at the Hospital.

MANCHESTER, 10. MONSALL HOSPITAL FOR INFECTIOUS DISEASES, NEWTON HEATH. MANCHESTER BABIES' AND CHILDREN'S HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER required. Salary £670 p.a., less deduction of £155 p.a., for residence, &c.

Applications, together with names of 3 referees, to be sent as soon as possible to Physician-Superintendent.

MANCHESTER, 20. WITHINGTON HOSPITAL. Manchester Regional Hospital Board. South Manchester Hospital Management Committee. The Board invite applications from registered practitioners for the post of MEDICAL REGISTRAR.

Applications, stating age, qualifications, present post, experience and names of 2 referees, to be forwarded to the Group Secretary at the Hospital, within 7 days of the appearance of this advertisement.

MANCHESTER, 20. CHRISTIE HOSPITAL AND HOLT RADIUM INSTITUTE. SOUTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICERS (radiotherapy) required. Appointments offer opportunity to acquire first-class experience in modern radiotherapy. Successful candidates will also have the opportunity of joining the course of instruction in radiotherapy which commences in April, 1954, offered by the Manchester University jointly with this Hospital for the Diploma in Radiotherapy of the Royal Colleges.

Applications to be forwarded immediately to the Group Secretary, Withington Hospital, Manchester, 20.

MANCHESTER REGIONAL HOSPITAL BOARD. South MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. The Board invite applications from registered medical practitioners for the post of RADIOTHERAPY REGISTRAR at the Christie Hospital and Holt Radium Institute.

Applications, stating age, qualifications, present post, experience, and names of 2 referees, to be forwarded to the undersigned immediately. A. H. KEATES, Secretary,

South Manchester Hospital Management Committee.

Withington Hospital, Manchester, 20.

MANCHESTER REGIONAL HOSPITAL BOARD. Sal- FORD HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT ANÆSTHETIST (Registrar grade) in the above Group. The post is recognised for the D.A. Experience in the administration of anæsthetics for all types of surgery is available in the hospitals of the Group. Candidates wishing to take advantage of these facilities may do so. Details will be supplied on request.

Applications, together with copies of 2 recent testimonials, should be sent to the Group Secretary, Salford Royal Hospital, Salford, 3, before 15th August, 1953.

MANCHESTER REGIONAL HOSPITAL BOARD invite applications for the non-resident post of REGISTRAR in Orthopædic Surgery, to the Blackpool and Fylde Group of hospitals, with main duties at Victoria Hospital, Blackpool.

Applications, with copies of 2 recent testimonials, to the Group Secretary, Blackpool and Fylde Hospital Management Committee, Victoria Hospital, Blackpool.

MANCHESTER REGIONAL HOSPITAL BOARD invite applications for the post of RESIDENT REGISTRAR in the Board's Non-tuberculous Thoracic Surgery Unit of 48 Beds based at Park Hospital, Davyhulme. National Health Service terms and conditions will apply. The successful candidate will be appointed for 1 year in the first instance and can take up the appointment immediately.

Application forms from the Secretary, West Manchester Hospital Management Committee, Park Hospital, Davyhulme.

MANCHESTER REGIONAL HOSPITAL BOARD. REGISTRAR (chest diseases) required to carry out duties arranged by the Consultant Chest Physician at the Altrincham Northwich, Crewe, and Hefferston Grange Sanatorium Chest Clinics.

Applications, together with 2 recent testimonials, should be sent to the Group Secretary, North and Mid-Cheshire Hospital Management Committee, The Hospital, Sinderland-road, Altrincham, Cheshire, not later than 10th August, 1953.

MANCHESTER REGIONAL HOSPITAL BOARD. REGISTRAR in General Medicine in the Bury and Rossendale Hospital Centre, with accommodation at Bury General Hospital.

Apply, giving full particulars and names of 2 referees, to—

H. WILKINSON, Group Secretary.

Bury General Hospital, Bury.

MANCHESTER. UNITED MANCHESTER HOSPITALS. MANCHESTER ROYAL EYE HOSPITAL. Applications are invited for RESIDENT MEDICAL STAFF (Senior House Officer grading—£670 p.a., less £130 p.a. for residential emoluments).

Application forms may be obtained from the undersigned.

H. R. NORTH, General Superintendent.

MANCHESTER. UNITED MANCHESTER HOSPITALS. MANCHESTER ROYAL EYE HOSPITAL. Applications are invited for the post of REGISTRAR (resident). Tenable for 12 months, subject to renewal. Previous experience in ophthalmology essential. The terms and conditions of service for hospital medical and dental staffs will apply.

Application forms may be obtained from the undersigned.

H. R. NORTH, General Superintendent.

MANCHESTER. UNITED MANCHESTER HOSPITALS. SAINT MARY'S HOSPITALS, MANCHESTER. Applications are invited from registered medical practitioners (Male or Female) for the post of HOUSE PHYSICIAN in the Neonatal Unit of Saint Mary's Hospitals (attached to the University Department of Child Health) for a period of 6 months, vacant on 8th September, 1953. Previous hospital experience essential and pædiatric experience desirable. Duties include the care of the newborn in the Maternity Department, the care of infants in the infants' ward and work in the clinics under the charge of the Department of Child Health. Salary in accordance with national scale.

Applications, stating qualifications and experience, together with the names of 3 referees, should be sent to the undersigned within 10 days of the appearance of this notice.

A. R. WISE, General Superintendent.

Saint Mary's Hospitals, Whitworth Park, Manchester, 13.

MANCHESTER. UNITED MANCHESTER HOSPITALS. MANCHESTER ROYAL INFIRMARY, MANCHESTER, 13. REGISTRAR to a General Medical Unit, to commence as soon as possible. Whole-time non-resident appointment, for 12 months, renewable. Applicants must possess higher qualifications.

Applications to be made on forms obtainable from the undersigned and to be returned not later than 19th August, 1953.

G. H. TAYLOR, Secretary.

MANCHESTER. UNITED MANCHESTER HOSPITALS. MANCHESTER ROYAL INFIRMARY, MANCHESTER, 13. REGISTRAR to the Department of Diagnostic Radiology, to commence as soon as possible. Whole-time appointment for 12 months, renewable. Applicants must possess the D.M.R.D. or its equivalent.

Applications to be made on forms obtainable from the undersigned and to be returned not later than 19th August, 1953.

G. H. TAYLOR, Secretary.

MANCHESTER. UNITED MANCHESTER HOSPITALS. MANCHESTER ROYAL INFIRMARY, MANCHESTER, 13. REGISTRAR to the Department of Hæmatology, to commence as soon as possible. Whole-time appointment for 12 months, renewable. The post is mainly clinical in character, involving ward and general outpatient clinic duties. Higher qualifications would be an advantage, but are not essential.

Applications to be made on forms obtainable from the undersigned and to be returned not later than 19th August, 1953.

G. H. TAYLOR, Secretary.

MANCHESTER (near). ROYAL MANCHESTER CHIL- DREN'S HOSPITAL, PENDLEBURY, near MANCHESTER. SALFORD HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from medical practitioners (Male or Female) for the post of RESIDENT HOUSE SURGEON (House Officer status) falling vacant on 8th August, 1953. The appointment is for a period of 6 months and is open to pre-registration graduates.

Applications, stating age, qualifications with dates, nationality, and accompanied by copies of 3 recent testimonials, to be sent to the Superintendent at the Hospital, to be received within 7 days of the appearance of this advertisement.

MANCHESTER, 8. SPRINGFIELD HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER at this Mental Hospital of 760 Beds. The Hospital is closely associated with the Department of Psychiatry of the University of Manchester, and is approved for the D.P.M. England and R.M.P.A. The admission-rate is substantial and a wide range of clinical material is available. Most forms of modern treatment are used. There are associated outpatient clinics. Accommodation is available for a single person, for which the appropriate deduction will be made. Permission to live out may be granted in certain circumstances.

Applications to the Medical Superintendent as soon as possible.

MANCHESTER, 8. CRUMPSALL HOSPITAL. (General Hospital—1225 Beds.) Applications are invited for the appointment of SENIOR HOUSE OFFICER (medicine), vacant on 13th September, 1953.

Applications, stating age, nationality, qualifications, and dates, particulars of previous appointments with dates, together with names and addresses of 2 referees, to be sent to the undersigned within 10 days of the appearance of this advertisement.

A. T. SAMPSON, Group Secretary.

Crumpsall Hospital, Manchester, 8.

MERTHYR TYDFIL. ST. TYDFIL'S HOSPITAL. (395 Beds.) MERTHYR AND ABERDARE HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the following posts :—

RESIDENT SENIOR HOUSE OFFICER in Obstetrics and Gynæcology. The successful applicant will be based at St. Tydfil's Hospital, Merthyr Tydfil, and work at obstetrics and gynæcology in the Merthyr Area. Applicants must have been registered not less than 1 year as a Medical Practitioner and have previously held house appointments.

HOUSE PHYSICIAN (resident). Appointment is for a period of 6 months.

Salary in accordance with the terms of service issued by the Ministry of Health.

Applications, with full particulars, should be sent to the Group Secretary, Merthyr and Aberdare Hospital Management Committee, St. Tydfil's Hospital, Merthyr Tydfil.

NUNEATON. MANOR HOSPITAL. (139 Beds.) House SURGEON for general surgical duties including E.N.T. and ophthalmic work. Recognised for F.R.C.S. ; pre-registration post.

Applications to the Hospital Secretary.

NUNEATON. MANOR HOSPITAL. (139 Beds.) Applications are invited for the post of HOUSE PHYSICIAN (32 general medical beds). Post vacant 1st August.

Applications to the Hospital Secretary.

NEWARK GENERAL HOSPITAL, Newark. Sheffield REGIONAL HOSPITAL BOARD. Whole-time RESIDENT SURGICAL HOUSE OFFICER with general duties required at Registrar rate of pay. This post offers good experience to anyone preparing to enter General Practice. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 10th August, 1953, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

NEWMARKET GENERAL HOSPITAL. East Anglian REGIONAL HOSPITAL BOARD. ANÆSTHETIC REGISTRAR. Post now vacant. Appointment for 1 year, renewable for second year.

Applications, stating age, qualifications, and details of present and previous appointments, together with names of 3 referees, to Secretary of Board, 117, Chesterton-road, Cambridge, by 10th August, 1953. Candidates invited to visit Hospital by direct arrangement with Hospital Management Committee Secretary at the Hospital.

NEWMARKET GENERAL HOSPITAL, Newmarket, SUFFOLK. Applications are invited for the post of HOUSE SURGEON, available immediately. Duties include surgical house charge of general surgical, E.N.T. and eye beds. The post is tenable for 6 months and is resident. Salary in accordance with national scale, less £100 p.a. for board and residence.

Applications, together with copies of 3 testimonials, should be addressed to the Physician-Superintendent.

NEWMARKET GENERAL HOSPITAL, Newmarket, SUFFOLK. Applications are invited for the post of HOUSE PHYSICIAN, vacant now. Duties include house charge of acute general medical and tuberculosis beds with some opportunity for anæsthetics under the supervision of the Consultant in anæsthesia. The post is tenable for 6 months, salary in accordance with national scale, less £100 for board and residence.

Applications, with copies of 3 recent testimonials, should be addressed to the Physician-Superintendent.

NEWPORT, I.W. ST. MARY'S HOSPITAL. (365 Beds.) ISLE OF WIGHT GROUP HOSPITAL MANAGEMENT COMMITTEE. CASUALTY OFFICER, vacant now. Salary £670, less £130 for accommodation and services. Model Casualty Department, newly constructed. Living accommodation for a married candidate would be made available if required.

Applications, with full details, to Chief Administrative Officer, Clatterford House, Carisbrooke, I.W.

NEWPORT, I.W. ST. MARY'S HOSPITAL. (365 Beds.) ISLE OF WIGHT GROUP HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER in Surgery. Salary £670 p.a. Applications are invited from registered medical practitioners.

HOUSE SURGEON. Post approved for Pre-registration Service. National salary scale and conditions. Vacant now.

Living accommodation for a married candidate would be made available if required.

Applications, stating age, nationality, qualifications, and experience, together with the names of 2 referees, to be sent as soon as possible to Chief Administrative Officer, Hospital Management Committee Headquarters, Clatterford House, Carisbrooke, I.W.

NEWPORT, MON. ROYAL GWENT HOSPITAL. (259 Beds. Recognised F.R.C.S.) 2 SENIOR HOUSE OFFICERS or HOUSE OFFICERS required for Casualty Department in August. Posts recognised F.R.C.S. for 6 months. Senior Hospital Medical Officer in full-time charge of Department, through which pass all medical and surgical emergencies. Attendances 48,000 annually. Excellent experience. Post tenable 6 or 12 months as desired.

Write, quoting 2 referees, to T. A. JONES.
64, Cardiff-road, Newport, Mon.

NEWPORT AND EAST MONMOUTHSHIRE GROUP. Vacancies for House Officers exist, all recognised for Pre-registration Service :—

Royal Gwent Hospital, Newport, Mon. (259 Beds)
HOUSE SURGEON (including Gynæcology). Recognised F.R.C.S.

Pontypool and District Hospital, Pontypool (115 Beds)
HOUSE PHYSICIAN (including Pædiatrics).
2 HOUSE SURGEONS (1 post recognised F.R.C.S.).

Write, quoting 2 referees, to T. A. JONES.
64, Cardiff-road, Newport, Mon.

NEWCASTLE. THE UNITED NEWCASTLE UPON TYNE HOSPITALS. ROYAL VICTORIA INFIRMARY. Applications are invited for the whole-time non-resident appointment of REGISTRAR in the Department of Radiotherapy. The possession of D.M.R. or D.M.R.T. is an advantage but not essential for this appointment, which will be for 1 year in the first instance.

Applications, giving full details and the names and addresses of 3 referees, should be sent to the undersigned within 2 weeks of the appearance of this advertisement.

A. W. SANDERSON, House Governor and Secretary.
Royal Victoria Infirmary, Newcastle upon Tyne.

NEWCASTLE. THE UNITED NEWCASTLE UPON TYNE HOSPITALS. ROYAL VICTORIA INFIRMARY. Applications are invited for the whole-time post of SENIOR REGISTRAR in the Department of Radiotherapy. Candidates should hold a recognised Diploma in Radiotherapy or a higher qualification in medicine or surgery.

Applications, giving age, nationality, experience and qualifications, with the names and addresses of 3 referees, should be sent to the undersigned within 2 weeks of the date of appearance of this advertisement.

A. W. SANDERSON, House Governor and Secretary.
Royal Victoria Infirmary, Newcastle upon Tyne.

NEWCASTLE REGIONAL HOSPITAL BOARD. Gates-HEAD HOSPITAL MANAGEMENT COMMITTEE GROUP. Approximately 65 orthopædic beds in the Group. ORTHOPÆDIC REGISTRAR (whole-time) non-resident. Appointment up to 31st August, 1954, in the first instance after which date the appointment may be renewed for a further year. Salary scale £775–£890. The appointee will be required to undertake duties in the Casualty Department, Queen Elizabeth Hospital, &c.

Applications, together with names and addresses of referees (preferably) or testimonials to a total of 3, to be sent to the Senior Administrative Medical Officer, "Blythswood South," Osborne-road, Newcastle upon Tyne, 2, within 14 days.

NEWCASTLE REGIONAL HOSPITAL BOARD. New-CASTLE GENERAL HOSPITAL. (890 Beds, including 100 Beds, obstetric and gynæcological.) REGISTRAR OBSTETRICIAN AND GYNÆCOLOGIST (whole-time), required up to 31st August, 1954, in the first instance, after which date the appointment may be renewed for a further year. The successful applicant may be seconded for 6 months to the Hexham Group of hospitals, resident at Dilston Hall Maternity Hospital. This Unit is associated with the Newcastle General Hospital Unit. Salary scale £775–£890.

Applications, together with names and addresses of referees (preferably), or testimonials to a total of 3, to be sent to the Senior Administrative Medical Officer, "Blythswood South." Osborne-road, Newcastle upon Tyne, 2, within 14 days.

NEWCASTLE GENERAL HOSPITAL. (861 Beds.) NEWCASTLE UPON TYNE HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for a Whole-time SENIOR HOUSE OFFICER (pædiatrics), to the Children's Department in the above Hospital, to commence duty on 1st September, 1953. Salary is in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales). This department is actively associated with the Department of Child Health of Durham University, and the post offers good opportunities for gaining experience in many aspects of pædiatrics The appointment is for 1 year in the first instance.

Applications, together with 1 copy of 2 testimonials, to be sent to the Secretary, Newcastle General Hospital, Westgate-road, Newcastle upon Tyne, 4.

NEWCASTLE GENERAL HOSPITAL. (861 Beds.) NEWCASTLE UPON TYNE HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the resident post of SENIOR HOUSE OFFICER (general surgical wards), which becomes vacant during August, 1953. The appointment is tenable for 12 months in the first instance. This post is recognised by the Royal College of Surgeons under the F.R.C.S. regulations.

Applications should be addressed to the Secretary, Newcastle General Hospital, Westgate-road, Newcastle upon Tyne, 4, together with 1 copy of 2 recent testimonials by 17th August, 1953.

NORTHAMPTON. MANFIELD ORTHOPÆDIC HOS-PITAL. NORTHAMPTON AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of ORTHOPÆDIC SENIOR HOUSE OFFICER (resident), vacant now. The appointment will be for about 1 year. Salary £670 p.a., with a deduction of £100 p.a. for residential emoluments. The post provides experience in a wide range of orthopædic treatment, including outpatient clinics.

Applications, stating age, nationality, qualifications, and experience, together with copies of testimonials, should be sent immediately to the Secretary, Northampton Management Committee, General Hospital, Northampton.

NORWICH. NORFOLK AND NORWICH HOSPITAL. (440 Beds.) Applications are invited for the appointment of SENIOR HOUSE SURGEON to the Orthopædic Department. Salary £670 p.a., less £150 p.a. for full residential emoluments.

Applications, stating age, qualifications, experience, with names of 2 referees, to Secretary, Group 6 Hospital Management Committee, St. Stephen's-road, Norwich.

NOTTINGHAM AND MIDLAND EYE INFIRMARY. NOTTINGHAM NO. 1 HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON (resident) required at the above Infirmary. Salary and conditions of service in accordance with the published conditions of the Ministry of Health. Duties to commence as soon as possible. This post is recognised for the D.O.M.S. examination.

Applications, stating age, qualifications and experience, together with copies of testimonials, to be sent to—

H. M. STANLEY, Secretary.
General Hospital, Nottingham.

NOTTINGHAM GENERAL HOSPITAL. Required, SENIOR MEDICAL HOUSE OFFICER for the above Hospital ; duties to commence about the beginning of September, 1953. Salary (less £150 residential emoluments) and conditions of service in accordance with those laid down by the Ministry.

Applications, stating age, qualifications and experience, together with copies of testimonials, to be sent to—
General Hospital, Nottingham. HENRY M. STANLEY.

NOTTINGHAM GENERAL HOSPITAL. 2 Resident HOUSE SURGEONS required (Male or Female) for the above Hospital, duties to commence as soon as possible. Salary and conditions of service in accordance with published regulations. If held by R practitioners the appointments will be for a period of 6 months.

Applications, stating age, qualifications and experience, together with copies of testimonials, to be sent to—
HENRY M. STANLEY, Group Secretary.

NOTTINGHAM GENERAL HOSPITAL. Applications are invited from registered medical practitioners for the post of ORTHOPÆDIC AND FRACTURE SENIOR HOUSE OFFICER. The post offers exceptional experience in traumatic and orthopædic surgery. Duties to commence as soon as possible. Salary and conditions of service in accordance with Ministry regulations. If resident £150 deducted for emoluments.

Applications, stating age, qualifications and experience, together with copies of testimonials, to be sent to—
HENRY M. STANLEY, Secretary.

NOTTINGHAM GENERAL HOSPITAL. Applications are invited for the post of RESIDENT CLINICAL PATHOLOGIST (Senior House Officer grade), vacant 1st October. Previous experience in pathology not essential. Opportunities for training in all branches of clinical pathology are afforded in a Department serving over 1200 Beds. Salary and conditions of service in accordance with Ministry regulations.

Applications, stating age, qualifications and experience, together with names and addresses of referees, to be sent to the undersigned before 22nd August.

HENRY M. STANLEY, Group Secretary.

NOTTINGHAM GENERAL HOSPITAL. Sheffield REGIONAL HOSPITAL BOARD. Whole-time RESIDENT or NON-RESIDENT REGISTRAR (orthopædics) required. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 17th August, 1953, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

OLDHAM. BOUNDARY PARK GENERAL HOSPITAL. (390 Beds—Recognised for F.R.C.S.) Applications are invited for the appointment of HOUSE SURGEON (general—recognised for pre-registration purposes), vacant immediately.

Applications, containing details of qualifications and experience, together with copies of 2 recent testimonials and quoting Ref. No. B/112, should be forwarded to the Group Secretary, Oldham and District Hospital Management Committee, Central Offices, Rochdale-road, Oldham.

OLDHAM ROYAL INFIRMARY. (190 Beds—Recognised for F.R.C.S.) Applications are invited for the appointment of HOUSE SURGEON (general—recognised for pre-registration purposes), vacant immediately.

Applications, containing details of qualifications and experience, together with copies of 2 recent testimonials and quoting Ref. No. B/113, should be forwarded to the Group Secretary, Oldham and District Hospital Management Committee, Central Offices, Rochdale-road, Oldham.

OSWESTRY. THE ROBERT JONES AND AGNES HUNT ORTHOPÆDIC HOSPITAL. SENIOR SURGICAL HOUSE OFFICER (resident) required at once. Appointment in the first place for 6 months with a possibility of extension.

Applications, with copies of 2 recent testimonials, to be sent to the Secretary.

OTLEY. THE GENERAL HOSPITAL. Ilkley and Otley HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON (pre-registration post) with duties commencing 1st August, 1953. 170-Bedded hospital staffed by Consultants who are members of the Teaching staff of the University of Leeds.

Applications to the Group Secretary, The General Hospital, Otley, Yorks.

OXFORD. UNITED OXFORD HOSPITALS. Applications are invited for post of HOUSE SURGEON to the Department of Radiotherapy at the Churchill Hospital for 6 months with immediate effect.

Applications, stating age, experience and qualifications, together with names of 2 referees, should be sent to Administrator, Radcliffe Infirmary, Oxford.

PONTYPOOL AND DISTRICT HOSPITAL, Pontypool, MON. (115 Beds.) JUNIOR HOSPITAL MEDICAL OFFICER (surgical). This is the senior resident post. 2 House Surgeons and a House Physician also resident. Salary £700–£50–£1000, less £150 board-residence.

Write, quoting 2 referees, to T. A. JONES.
64, Cardiff-road, Newport, Mon.

PORTSMOUTH GROUP HOSPITAL MANAGEMENT COMMITTEE. INFECTIOUS DISEASES HOSPITAL. (310 Beds.) Applications are invited for the appointment of HOUSE PHYSICIAN, whose work will comprise duties in both infectious diseases and tuberculosis wards.

Applications, stating age, experience, and qualifications, and names of 2 referees, should be submitted as soon as possible to—
35, Grove-road South, Southsea. E. H. HURST.

PORTSMOUTH GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the following appointments :—

St. Mary's Hospital (General Hospital with 150 surgical beds—recognised for the F.R.C.S.)
SENIOR HOUSE OFFICER (Casualty and Orthopædic Departments), vacant now.
HOUSE PHYSICIAN, vacant 10th September.

Royal Portsmouth Hospital (General Hospital with 70 surgical beds and 68 orthopædic beds—recognised for the F.R.C.S.)
HOUSE SURGEON (general surgery and orthopædics), vacant 15th August.

Queen Alexandra Hospital (124 surgical beds and 21 E.N.T. beds)
SENIOR HOUSE SURGEON (E.N.T. and general surgery), vacant 8th September.

Applications, stating age, experience and qualifications, together with the names of 2 referees, should be submitted as soon as possible to E. H. HURST.
35, Grove-road South, Southsea.

PORTSMOUTH GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment, vacant now, of REGISTRAR in the Chest Services of the Group for duties at the Portsmouth Chest Clinic and the tuberculosis wards at the Infectious Diseases Hospital and St. Mary's Hospital, Portsmouth, including experience with a major Thoracic Surgery Unit.

Forms of application may be obtained from the Secretary, Portsmouth Group Hospital Management Committee, 35, Grove-road South, Southsea, which should be returned to him duly completed on or before 14th August, 1953. Canvassing will disqualify. Candidates may visit the above Clinic and Hospitals by arrangement with the Group Secretary.

PAISLEY. THE ROYAL ALEXANDRA INFIRMARY. The undernoted posts will become vacant on 1st August, 1953 :—
(1) HOUSE SURGEON for the Orthopædic and Fracture Unit.
(2) HOUSE SURGEON for general surgical wards.

Applications should be addressed to the Group Medical Superintendent, at the above Hospital.

PETERBOROUGH. MEMORIAL HOSPITAL. Peter-BOROUGH AND STAMFORD HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the position of HOUSE PHYSICIAN, which will become vacant on 23rd August, 1953. The appointment will be for 6 months.

Applications, with testimonials, should be addressed to the Secretary, The Memorial Hospital, Midland-road, Peterborough.

PETERBOROUGH MEMORIAL HOSPITAL AND ANNEXES. EAST ANGLIAN REGIONAL HOSPITAL BOARD. MEDICAL REGISTRAR. Post provides experience in general medicine, pædiatrics and infectious diseases. Appointment for 1 year, renewable for second year.

Applications, stating age, qualifications, and details of present and previous appointments, with names of 3 referees, to Secretary of Board, 117, Chesterton-road, Cambridge, by 17th August, 1953. Candidates invited to visit hospitals by arrangement with Hospital Management Committee Secretary at the Hospital.

PENZANCE. WEST CORNWALL HOSPITAL. (General —100 Beds.) WEST CORNWALL HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from pre-registration graduates or qualified medical practitioners for the post of HOUSE SURGEON.

Applications, stating age, nationality, qualifications and experience, and enclosing copies of 2 recent testimonials, should be forwarded to the Hospital Secretary, West Cornwall Hospital, Penzance.

PLYMOUTH. SOUTH DEVON AND EAST CORNWALL HOSPITAL. Applications invited from registered medical practitioners for the appointments of :—
(1) SENIOR HOUSE OFFICER to Casualty and Fracture Department, Greenbank Road Section, vacant immediately.
(2) SENIOR HOUSE OFFICER in Surgery, Greenbank Road Section, vacant 9th October, 1953, recognised for the Fellowship of the Royal College of Surgeons.
(3) RESIDENT ANÆSTHETIST, Greenbank Road Section, vacant immediately, recognised for the D.A.
(4) HOUSE SURGEONS, Greenbank Road Section, vacancies 13th September, 17th and 20th October, 1953, recognised for the Fellowship of the Royal College of Surgeons.
(5) SENIOR HOUSE OFFICER in Surgery, Freedom Fields Section, vacant immediately, recognised for the Fellowship of the Royal College of Surgeons.
(6) HOUSE PHYSICIAN, Freedom Fields Section, vacant 1st September, 1953.
(7) HOUSE OFFICER in Obstetrics, Alexandra Maternity Home, Devonport, vacant immediately.

Applications, stating age, nationality, qualifications, and experience, with the names of 3 referees, to be sent to the undersigned as soon as possible.

ARTHUR R. CASH, Group Secretary.
7, Nelson-gardens, Stoke, Devonport.

PLYMOUTH CLINICAL AREA. The Board of Governors OF THE UNITED BRISTOL HOSPITALS AND THE SOUTH-WESTERN REGIONAL HOSPITAL BOARD. Applications are invited by the above Boards from registered medical practitioners for the joint appointment of SENIOR REGISTRAR in Psychiatry to the Plymouth Clinical Area, based on Moorhaven Hospital, Ivybridge, South Devon. The appointment will be held for 1 year in the first instance and, subject to satisfactory service, will be renewable annually for a further period not exceeding 4 years in all. Applicants must have had previous experience in psychiatry and preference will be given to holders of the Diploma in Psychological Medicine. An excellent maisonette is available suitable for a married man with children. The post offers opportunities in all branches of inpatient and outpatient clinical work, including neurology, mental deficiency, and child guidance. The outpatient service is based on the South Devon and East Cornwall Hospital, Plymouth, and the Plymouth Child Guidance Clinic. Experience can be gained in the principles and practice of psychotherapy under supervision as well as in the physical methods of treatment, and half the time given to outpatient work is devoted to treatment. Moorhaven Hospital is recognised as a training centre for the R.M.P.A. D.P.M. A copy of the 1952 Annual Report and further particulars can be obtained from the Physician-Superintendent, Moorhaven Hospital.

Applications (12 copies), stating date of birth, qualifications, and experience, together with 12 copies of 2 testimonials, and the names and addresses of 2 referees, should be sent to the Secretary of the Regional Hospital Board, 27, Tyndalls Park-road, Bristol, 8, not later than 15th August, 1953.

ROMFORD, ESSEX. OLDCHURCH HOSPITAL. (722 Beds.) Applications are invited for the post of RESIDENT HOUSE SURGEON in the General Surgical Unit. Recognised for F.R.C.S. 6 months appointment. This very active General Surgical Unit of approximately 100 Beds affords ample opportunity for candidates to obtain first-class tuition and experience.

Applications, stating age, nationality, qualifications with dates, and details of experience, together with copies of 2 recent testimonials or names of 2 referees, should be sent immediately to the Group Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford.

ROMFORD, ESSEX. OLDCHURCH HOSPITAL. (722 Beds.) Applications are invited from registered medical practitioners for the post of SENIOR HOUSE OFFICER in the Department of Ophthalmology.

Applications, stating age, qualifications, present appointment and experience with dates, together with copies of 2 testimonials of recent date or names of 2 referees, should be sent immediately to the Group Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford.

ROMFORD, ESSEX. OLDCHURCH HOSPITAL. Applications are invited from registered medical practitioners for the post, now vacant, of SENIOR HOUSE OFFICER (resident) for duties in the Casualty and Admissions Department at the above Hospital. This is a large general hospital, with specialised departments dealing with all types of acute medical and surgical cases. The post affords good opportunity for gaining tuition and experience.

Applications should be addressed immediately to the Secretary of the Romford Group Hospital Management Committee, Oldchurch Hospital, Romford, stating age, nationality, qualifications, experience, and 2 testimonials of recent date or names of 2 referees.

ROMFORD, ESSEX. VICTORIA HOSPITAL. (91 Beds.) Applications are invited from registered medical practitioners (Male) for the post of RESIDENT HOUSE PHYSICIAN vacant from 16th August, 1953. The duties will include experience in gynæcology. 6 months appointment.

Applications, stating age, nationality, qualifications with dates, and experience, together with copies of 2 recent testimonials or names of 2 referees, should be sent immediately to the Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford.

REDRUTH. CAMBORNE-REDRUTH HOSPITAL. (151 Beds—4 Residents.) WEST CORNWALL HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (surgical) required for the above Hospital. Post vacant 7th August, 1953. This is a general hospital with a great variety of cases. The post gives good experience in diagnosis, operative and postoperative treatment, and in actual operative procedure to the candidate.

Applications, stating age, experience and nationality, together with references, to Hospital Secretary, Camborne-Redruth Hospital, Redruth, Cornwall.

REDHILL. EAST SURREY HOSPITAL, Shrewsbury-road, REDHILL, SURREY. (139 Beds.) REDHILL GROUP HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (Male). Duties mainly surgical, with some medicine.

Apply, stating the names of 2 referees or testimonials, to Hospital Secretary.

ROCHDALE. BIRCH HILL HOSPITAL. (General— 951 Beds.) ROCHDALE AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (anæsthetics). Appointment for 1 year and post recognised for D.A.

Applications to Group Secretary, Central Offices, Birch Hill Hospital, Rochdale, not later than 8th August, 1953.

RUGBY (near). ST. MARY'S HOSPITAL, Harborough MAGNA, near RUGBY. HOUSE SURGEON required (gynæcological and obstetric). Post vacant 31st August.

Applications to the Secretary, Group 20, Hospital Management Committee, Coventry and Warwickshire Hospital, Coventry.

RYDE, I.W. ROYAL I.W. COUNTY HOSPITAL. CASUALTY OFFICER/ORTHOPÆDIC HOUSE SURGEON (Senior House Officer grade—£670 p.a.). Active Surgical Department with considerable amount of traumatic surgery, with care of orthopædic beds.

Applications, stating age, qualifications, experience and names of 2 referees, to Group Secretary, Hospital Management Committee, Clatterford House, Carisbrooke, I.W.

STOKE-ON-TRENT. CITY GENERAL HOSPITAL. STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of HOUSE OFFICER (medical), 4 posts vacant shortly. Posts recognised for experience during pre-registration period.

Apply, with copy testimonials, stating age, nationality, and full details of previous service, to the Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent.

STOKE-ON-TRENT. CITY GENERAL HOSPITAL. STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointments of HOUSE SURGEONS (Male or Female), pre-registration posts. 3 posts becoming vacant during the months of August and September and tenable for 6 months. Posts approved for F.R.C.S. examination.

Applications, stating age, nationality and qualifications with dates, together with copy testimonials, to the Group Secretary, Stoke-on-Trent Hospital Management Committee, Princes-road, Stoke-on-Trent, as soon as possible.

STOKE-ON-TRENT. CITY GENERAL HOSPITAL. STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. Locum ANÆSTHETIST required owing to temporary shortage of staff. Salary according to status and experience.

Applications to the Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent.

STOKE-ON-TRENT. CITY GENERAL HOSPITAL. STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of SENIOR HOUSE OFFICER in Paediatrics. Post recognised for D.C.H.

Applications, with copy testimonials, and details of previous experience, should be forwarded to the Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent, as soon as possible.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of HOUSE OFFICER (medical) pre-registration post, vacant 1st September, 1953.

Applications, giving full details, together with copy testimonials, to the Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent.

STOKE-ON-TRENT. NORTH STAFFS ROYAL INFIRMARY. (475 Beds.) STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. Applications invited for post of SENIOR HOUSE OFFICER (ophthalmics), now vacant. Recognised for F.R.C.S. and D.O.

Applications, stating age, and experience, together with copy testimonials, to the Group Secretary at Head Office, Hospital Management Committee, Princes-road, Stoke-on-Trent.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of HOUSE OFFICER (general surgery), vacant shortly. The Hospital is recognised for F.R.C.S. examination and the post is recognised for experience during pre-registration period.

Apply, with copy testimonials, stating age, nationality, and full details of previous service, to the Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. HOUSE OFFICER (orthopædics) required, vacant now. Post recognised for F.R.C.S.

Applications, stating age and nationality, together with details of previous service, to the Group Secretary, Stoke-on-Trent Hospital Management Committee, Princes-road, Stoke-on-Trent.

STOKE-ON-TRENT HOSPITAL MANAGEMENT COM-MITTEE. ORTHOPÆDIC HOSPITAL, HARTSHILL. Applications are invited for the post of SENIOR HOUSE OFFICER (orthopædics), vacant now.

Applications, stating age, and nationality, together with details of previous service, to the Group Secretary, Stoke-on-Trent Hospital Management Committee, Princes-road, Stoke-on-Trent.

SOUTHAMPTON CHILDREN'S HOSPITAL. (Recog-nised by Conjoint Board for D.C.H.) HOUSE OFFICER required; post vacant 24th August, 1953. Salary, &c., as nationally advocated. Preference given to candidates intending to specialise in pædiatrics.

Applications, with copies of testimonials, to be submitted not later than 6th August, 1953, to the Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON GENERAL HOSPITAL. (471 Beds.) SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of Whole-time RESIDENT REGISTRAR in Anæsthetics. Candidates may visit the Hospital if they so desire.

Forms of application, which should be returned to the undersigned by not later than 15th August, 1953, will be forwarded on receipt of a stamped, addressed envelope.

FRANK JENNINGS, Group Secretary,
Southampton Group Hospital Management Committee.
Bullar-street, Southampton.

SOUTHAMPTON GENERAL HOSPITAL. (80 surgical beds.) HOUSE SURGEON (resident) required early September. Post tenable for 6 months. Recognised for F.R.C.S. and for Pre-registration Service.

Applications, with copies of testimonials, should be forwarded as soon as possible to the Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON GROUP HOSPITAL MANAGEMENT COMMITTEE. HOUSE PHYSICIAN (resident) required for duties in the Southampton Group of Hospitals, from 1st September. Post tenable 6 months.

Applications, with copies of testimonials, should be forwarded as soon as possible to the Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL. (278 Beds.) CASUALTY OFFICER/SENIOR HOUSE OFFICER (orthopædic) required for the above Hospital (Orthopædic Unit, 74 Beds). This Hospital is the centre to which all trauma from a large industrial town and port is directed, thus providing excellent experience in the treatment of traumatic conditions.

Applications, with copies of testimonials, to be submitted as soon as possible to the Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON. ROYAL SOUTH HANTS HOS-PITAL. (278 Beds.) Recognised for F.R.C.S. CASUALTY OFFICER (Senior House Officer grading) required for the above Hospital.

Applications, with copies of testimonials, to be submitted as soon as possible to the Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time NON-RESIDENT REGISTRAR (anæsthetics) required at the City General Hospital, Sheffield. This is a large general hospital with a Department of Thoracic Surgery, a Regional Cardiological Centre and a Professorial Gynæcological Unit. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 17th August, 1953, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time SENIOR REGISTRARS in Psychiatry required for Bracebridge Heath Hospital, near Lincoln, The Pastures Hospital, Mickleover, near Derby, and The Towers Hospital, Humberstone, near Leicester. Posts non-resident at Bracebridge Heath Hospital and the Towers Hospital; accommodation for single or married person available at the Pastures Hospital. Appointments for 1 year in the first instance reviewable annually. Opportunity for research and experience in those special branches of psychiatry available in the Hospital area.

Application forms and details of posts obtainable from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 17th August, 1953.

SHEFFIELD REGIONAL HOSPITAL BOARD. Locum SURGICAL REGISTRAR required at the Grimsby General Hospital from 7th September to 26th October, 1953, inclusive. Remuneration at the rate of £16 per week.

Applications, giving names of 2 referees, should be sent to the Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time NON-RESIDENT SENIOR ORTHOPÆDIC REGISTRAR (transitional appointment) required for 1 year only at Doncaster Royal Infirmary. Terms as recently agreed by the Ministry of Health and the profession. Applications invited from Senior Orthopædic Registrars in fourth or subsequent years and from those who held such posts for 3 or more years but vacated them after 1st January, 1951.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, 10, by 17th August, 1953, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. Applications are invited for the post of NON-RESIDENT REGISTRAR in General Medicine at the Royal Hospital Unit.

Applications, stating age, qualifications and experience, with the names of 3 referees, should be sent to the Chief Administrative Officer, The United Sheffield Hospitals, West-street, Sheffield, 1, immediately.

SALISBURY GENERAL HOSPITAL. Salisbury Group HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of RESIDENT HOUSE SURGEON or SENIOR HOUSE OFFICER to the Orthopædic Department. Post offers experience in Plastic Unit in addition. Post vacant now and is graded according to experience.

Apply immediately, naming 2 referees, to Group Secretary, Odstock Hospital, Salisbury.

SALFORD ROYAL HOSPITAL. Salford Hospital Management COMMITTEE. SENIOR MEDICAL HOUSE OFFICER. Appointment for 1 year. Salary subject to a deduction of £155 p.a. for board and lodging. Vacant August.

Applications, with copies of 3 recent testimonials, should be sent to the Secretary, Salford Royal Hospital, Salford, 3.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited for 1 post as SENIOR REGISTRAR and 2 posts as REGISTRAR in Radiotherapy at the Royal Infirmary of Edinburgh. This Department is under the direction of the Professor of Radiotherapy of the University of Edinburgh and, apart from being the main centre for treatment in the South-Eastern Region, also accepts cases from other parts of Scotland. The posts are superannuable, and the conditions of service are in accordance with the regulations.

Applications, giving particulars of age, qualifications and previous experience, together with the names of 3 referees, should be submitted to the Secretary, South-Eastern Regional Hospital Board, Scotland, 11, Drumsheugh-gardens, Edinburgh, 3, within 30 days.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited for the temporary appointment, for a period of 12 months, of an ASSISTANT TUBERCULOSIS PHYSICIAN for duty in the Royal Victoria Dispensary, Edinburgh, this being the main centre for the outpatient treatment of tuberculosis in Edinburgh. The person appointed will be accorded the status of Senior Registrar and remunerated at the rate of £1000 p.a. The post is superannuable, and the conditions of service are in accordance with the regulations.

Applications, giving particulars of age, previous experience and qualifications, together with the names of 3 referees, should be submitted to the Secretary, South-Eastern Regional Hospital Board, Scotland, 11, Drumsheugh-gardens, Edinburgh, 3, within 30 days.

SCOTLAND. NORTHERN REGIONAL HOSPITAL BOARD. Applications are invited for a whole-time post of MEDICAL REGISTRAR at the Inverness Hospitals. The duties are mainly at Raigmore Hospital, Inverness.

Schedules of application and further particulars are obtainable from the undersigned, with whom applications should be lodged by 29th August, 1953. A. M. FRASER, M.D.
Secretary and Administrative Medical Officer.
Office of the Northern Regional Hospital Board,
Raigmore, Inverness.

ST. ALBANS CITY HOSPITAL. (372 Beds.) North West METROPOLITAN REGIONAL HOSPITAL BOARD. Whole-time GYNÆCOLOGICAL AND OBSTETRIC REGISTRAR required for duties mainly at the above Hospital which may be visited by direct appointment.

Application forms obtainable from, and returnable to, the Group Secretary, St. Albans City Hospital, Normandy-road, St. Albans, Herts, by 14th August, 1953.

ST. ALBANS. HILL END HOSPITAL. North West METROPOLITAN REGIONAL HOSPITAL BOARD. Whole-time PSYCHIATRIC REGISTRAR required at above Hospital. Post vacant 18th August, 1953. Successful candidate will be required to work whole-time on the wards, but will be given scope for the care of neurosis cases. Preference will be given to candidates able to conduct original research or who wish to study for higher qualifications. Hospital may be visited by direct appointment.

Application forms obtainable from, and returnable to, the Group Secretary, Mid Herts Group Hospital Management Committee, St. Albans City Hospital, Normandy-road, St. Albans, Herts, by 7th August, 1953.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for a whole-time appointment as RESIDENT SURGICAL OFFICER to fill a vacancy in the approved establishment at the Canterbury Group of hospitals. The salary will be £890 p.a. and the appointment will be in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales) and will be for 1 year in the first instance, renewable for a further year.

Applications, giving particulars of age, qualifications and experience, with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, not later than 15th August, 1953.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as Whole-time REGISTRAR in General Medicine to fill a vacancy in the approved trainee establishment at the Bromley Group of hospitals. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales), and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications and experience, with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, not later than 15th August, 1953.

SHREWSBURY. ROYAL SALOP INFIRMARY AND COPTHORNE HOSPITAL. (500 Beds.) SHREWSBURY GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of GYNÆCOLOGICAL HOUSE SURGEON (Male or Female). There are 50 gynæcological beds and 2 House Surgeons. The post is recognised for the M.R.C.O.G.

Applications, stating age, qualifications, nationality and experience, accompanied by copy testimonials, should be sent to— J. P. MALLETT, Group Secretary,
Group 15 Hospital Management Committee.
Royal Salop Infirmary, Shrewsbury, 10th July, 1953.

SHREWSBURY. ROYAL SALOP INFIRMARY. (241 Beds.) SHREWSBURY GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from general registered practitioners (Male or Female) for the appointment of RESIDENT HOUSE SURGEON in General Surgery. Vacant immediately, and tenable in the first instance for 6 months. Recognised for the F.R.C.S., and approved for pre-registration service. Salary and conditions of service in accordance with national scale.

Applications with references, should be sent to—
J. P. MALLETT, Group Secretary,
Group 15 Hospital Management Committee.
Royal Salop Infirmary, Shrewsbury, 27th July, 1953.

SHREWSBURY. ROYAL SALOP INFIRMARY. (241 Beds.) SHREWSBURY GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the appointment of ORTHOPÆDIC/ACCIDENT HOUSE SURGEON (Senior House Officer). The successful applicant will be allowed to attend for 2 days a month at The Robert Jones and Agnes Hunt Orthopædic Hospital, Oswestry, for postgraduate study with the Consultant. The post is recognised under the revised Fellowship regulations in respect of the 6 months training required of candidates for the Final Fellowship examination.

Applications, stating age, qualifications, nationality and experience, accompanied by copy testimonials, should be sent to— J. P. MALLETT, Group Secretary,
Group 15 Hospital Management Committee.
Royal Salop Infirmary, Shrewsbury, 10th July, 1953.

ST. HELENS. ECCLESTON HALL HOSPITAL. (75 Beds.) Applications are invited from suitably qualified registered medical practitioners for the post of SENIOR HOUSE OFFICER at the above Hospital. Salary in accordance with the terms and conditions of service for medical staff. The person appointed will work under the supervision of the Consultant Chest Physician for the Group. There are 75 Beds and the work comprises all types of tuberculosis. Good residential accommodation for a single person, male or female, is available.

Applications to be forwarded to the undersigned immediately.
N. RICHARDS, Secretary,
St. Helens and District Hospital Management Committee.
Group Office, County Hospital, Whiston, near Prescot.

STAFFORD. STAFFORDSHIRE GENERAL INFIRMARY. (159 Beds—Recovery Unit 32 Beds.) STAFFORD HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON (Male or Female). Post recognised for Pre-registration Service and for F.R.C.S.Eng.

Applications, giving full particulars, together with copies of 3 recent testimonials, to be forwarded to the Group Secretary, 13, Foregate-street, Stafford.

STAFFORD HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (anæsthetics), Male or Female. Recognised for D.A. Post now vacant. Duties mainly at the General Infirmary, Stafford, which is the main and acute general hospital of the Group.

Applications, with copies of 3 testimonials, to the Group Secretary, Stafford Hospital Management Committee, 13, Foregate-street, Stafford.

STRATFORD-ON-AVON HOSPITAL, Arden-street, STRATFORD-ON-AVON. Locum SURGICAL OFFICER required for 3 weeks from 24th August.

Applications to Hospital Secretary.

STOCKPORT. STEPPING HILL HOSPITAL. (Recognised for D.Obst.R.C.O.G.) Applications are invited for the post of HOUSE OFFICER (obstetrics and gynæcology). The post, which is resident, becomes vacant 1st September, 1953, at the above Hospital, which provides 73 Beds for obstetrics and 36 beds for gynæcology.

Applications, stating age, qualifications and experience, together with copies of 2 testimonials, or the names of 2 referees, to be addressed to the Secretary, Stockport and Buxton Hospital Management Committee, 59B, Shaw-heath, Stockport, immediately.

SOUTHEND GENERAL HOSPITAL. Required, Temporary SENIOR REGISTRAR to the Diagnostic X-ray Department at the above Hospital. Post vacant late August. The appointment is for a period of 6 months in the first instance, and thereafter on a month-to-month basis. Salary in accordance with that of Senior Registrar grade from £1000 to £1300 p.a., according to past experience in that grading. The appointment is non-resident.

Applications, stating age, qualifications and experience, together with copies of 3 recent testimonials, should reach the undersigned as soon as possible. J. C. FIELD, Secretary.

SLOUGH. UPTON HOSPITAL. Casualty Officer (House Officer grade) required immediately.

Applications, stating age, and qualifications, together with names of 2 referees, should be sent to the Hospital Secretary.

SLOUGH. UPTON HOSPITAL. Locum House Surgeon required for period 9th–22nd August.

Applications, stating qualifications, and previous experience, together with testimonials, should be sent to the Hospital Secretary.

SOUTHALL, MIDDLESEX. ST. BERNARD'S HOSPITAL FOR NERVOUS AND MENTAL DISORDERS. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR required at above Hospital. Hospital undertakes all modern psychiatric treatments both physical and psychotherapeutic, and the medical staff conduct several psychiatric outpatient clinics. Hospital may be visited by direct appointment.

Application forms obtainable from, and returnable to, the Group Secretary, St. Bernard's Hospital Management Committee, St. Bernard's Hospital, Southall, Middlesex, by 15th August, 1953.

SWINDON HOSPITALS. (500 Beds.) Applications invited for RESIDENT HOUSE PHYSICIANS in acute Medical Unit of 64 Beds at St. Margaret's Hospital. Posts recognised for training under pre-registration internship regulations.

Full details, together with copies of 3 recent testimonials, to Secretary, Swindon and District Hospital Management Committee, 7, Okus-road, Swindon, Wilts, as soon as possible.

SWANSEA HOSPITAL. (403 Beds.) Glantawe Hospital MANAGEMENT COMMITTEE. Registered medical practitioners are invited to apply for the non-resident appointment of SENIOR HOUSE OFFICER in the Orthopædic Department of Swansea Hospital. The Hospital is recognised for Part II of the Diploma in Physical Medicine.

Applications, stating age, qualifications and experience, should be addressed to— O. C. HOWELLS, Secretary,
Glantawe Hospital Management Committee.
Swansea Hospital, St. Helen's-road, Swansea.

SWANSEA HOSPITAL. (403 Beds.) Glantawe Hospital MANAGEMENT COMMITTEE. Registered medical practitioners are invited to apply for the resident post of SENIOR HOUSE OFFICER in the E.N.T. Department of the above Hospital. The Hospital is recognised under the regulations of the F.R.C.S. (E.N.T.) and the D.L.O.

Applications, stating age, qualifications and experience, should be forwarded to O. C. HOWELLS, Group Secretary.
St. Helen's-road, Swansea.

SWANSEA HOSPITAL. (403 Beds.) Glantawe Hospital MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the posts (2) of RESIDENT ANÆSTHETISTS (Senior House Officer grade). The Hospital is recognised under the D.A. regulations.

Applications, stating age, qualifications and experience, should be addressed to— O. C. HOWELLS, Group Secretary,
Glantawe Hospital Management Committee.
St. Helen's-road, Swansea.

SWANSEA. MOUNT PLEASANT HOSPITAL. (276 Beds.) GLANTAWE HOSPITAL MANAGEMENT COMMITTEE. Registered medical practitioners are invited to apply for the resident appointment of JUNIOR HOSPITAL MEDICAL OFFICER for work in the Medical and Surgical Departments, and in the chronic sick wards of the above Hospital.

Applications, stating age, experience and qualifications should be addressed to—
O. C. HOWELLS, Group Secretary,
Glantawe Hospital Management Committee.
St. Helen's-road, Swansea.

TAUNTON AND SOMERSET HOSPITAL. Taunton HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of SENIOR HOUSE OFFICER (gynæcology, 28 Beds; and obstetrics, 50 Beds). The appointment is for 6 months, renewable for a further 6 months, and preference will be given to candidates who have completed a 6 months appointment in obstetrics.

Applications, stating age, qualifications with dates, nationality, and details of experience, together with 2 recent testimonials, should be sent immediately to the Secretary, Musgrove Park Hospital, Taunton.

TAPLOW, near MAIDENHEAD. CANADIAN RED CROSS MEMORIAL HOSPITAL. HOUSE SURGEON required for post vacant 29th August, 1953; post recognised for the F.R.C.S. Preference will be given to persons seeking a pre-registration House Officer post under the Medical Act, 1950. Salary on national scale.

Applications, stating age, experience, and qualifications with dates, together with copies of 2 testimonials, should be sent to the Hospital Secretary by 7th August, 1953.

TRURO. ROYAL CORNWALL INFIRMARY. (General Hospital—212 Beds. 9 Residents.) WEST CORNWALL HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the 2 posts of SENIOR RESIDENT HOUSE OFFICER to the Orthopædic and Traumatic Department. This is a large and busy centralised unit with 2 Consultants, 64 Beds, and Outpatient Departments also 45-Bed Rehabilitation Annexe which deal with the whole of the West Cornwall Area. The posts are now vacant, and are tenable for 1 year.

Applications, stating age, nationality, qualifications and experience, and accompanied by copies of 2 recent testimonials, should be forwarded to the Hospital Secretary, Royal Cornwall Infirmary, Truro, without delay.

TUNSTALL. BURSLEM, HAYWOOD AND TUNSTALL WAR MEMORIAL HOSPITAL. (96 Beds.) STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of HOUSE OFFICER (general surgery).

Apply, with copy testimonials, stating age, nationality, and full details of previous service, to the Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent.

TUNSTALL. BURSLEM, HAYWOOD AND TUNSTALL WAR MEMORIAL HOSPITAL. (96 Beds.) STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of HOUSE OFFICER (medical).

Apply, with copy testimonials, and details of previous appointments held, to the Group Secretary, Stoke-on-Trent Hospital Management Committee, Princes-road, Stoke-on-Trent, as soon as possible.

TORQUAY. TORBAY HOSPITAL. Torquay District HOSPITAL MANAGEMENT COMMITTEE. RESIDENT SENIOR HOUSE OFFICER, with previous experience in surgery, required immediately. (Post recognised for F.R.C.S.)

Applications, stating qualifications, nationality, age, with copies of testimonials (quoting Ref. F.955/30), to be sent to the Group Secretary, Torquay District Hospital Management Committee, 62/64, East-street, Newton Abbot, S. Devon.

WALSALL GENERAL HOSPITAL, Staffs. Resident ANÆSTHETIST (Senior House Officer) required immediately. Post recognised for D.A., and tenable for 1 year.

Apply Secretary.

WARRINGTON GENERAL HOSPITAL. Applications are invited for the post of RESIDENT SENIOR HOUSE OFFICER (Male or Female—obstetrics and gynæcology), which will become vacant on 1st September, 1953. This post is recognised for the D.Obst.R.C.O.G. Scale of salary £670 p.a., less £130 for residential emoluments.

Applications, stating age, qualifications with dates, and details of experience, together with copies of recent testimonials, should be sent to the Group Secretary, Warrington and District Hospital Management Committee, c/o, General Hospital, Warrington.

WARRINGTON GENERAL HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER (pædiatrics), Male or Female, which will become vacant in early October next. Post recognised for D.C.H. Commencing salary £670 p.a., less £130 for residential emoluments.

Applications to be forwarded to—
H. L. BOOT, Group Secretary,
Warrington and District Hospital Management Committee.
c/o General Hospital, Warrington.

WARRINGTON INFIRMARY. (172 Beds.) Applications are invited for a vacancy at the above Hospital for a RESIDENT HOUSE SURGEON (Male or Female). Salary will be £350–£450 p.a., less a deduction of £100 for full residential emoluments.

Applications should be sent to—
H. L. BOOT, Group Secretary,
Warrington and District Hospital Management Committee.
c/o General Hospital, Warrington, Lancs.

WARWICK HOSPITAL. Applications are invited for the resident appointment of PÆDIATRIC HOUSE OFFICER (Male or Female) vacant 1st August. This post is recognised for pre-registration. 30-Bedded Pædiatric Unit. The Hospital is recognised for D.C.H.

Applications, with 2 recent testimonials, to the Administrative Officer, Warwick Hospital, Lakin-road, Warwick.

WARWICK (near). CENTRAL MENTAL HOSPITAL. SENIOR HOUSE OFFICER required in this Mental Hospital of 1400 Beds with Neurosis Unit, 4 adult and 2 child Psychiatric Clinics recognised for the D.P.M., and Departments of Electroencephalography, Occupational Therapy, Psychology and Social work. Salary £670 p.a. A modern house is available. Rental (inclusive of rates), £95 p.a.

Applications, together with the names and addresses of 3 referees, to the Medical Superintendent within 14 days of the appearance of this advertisement.

WATFORD. PEACE MEMORIAL HOSPITAL. North WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR in Pathology (non-resident) required in the Department of Morbid Anatomy at the Group Laboratory at above Hospital. Previous experience essential. Laboratory may be visited by direct appointment.

Application forms obtainable from, and returnable to, Group Secretary, West Herts Group Hospital Management Committee, 9, Rickmansworth-road, Watford, Herts, by not later than 10 days after the appearance of this advertisement.

WINCHESTER. ROYAL HAMPSHIRE COUNTY HOS-PITAL. (311 Beds.) SENIOR HOUSE OFFICER in the Pathological Department, vacant 2nd August. Preferably resident. Duties will include training in the various branches of clinical pathology, especially hæmatology. Previous experience in clinical pathology desirable, but not essential.

Applications, with copies of 2 testimonials, to the Secretary.

WINCHESTER. ROYAL HAMPSHIRE COUNTY HOS-PITAL. (311 Beds.) HOUSE PHYSICIAN to the Pædiatric Department, vacant 18th September. Preference will be given to applicants wishing to specialise in pædiatrics. The department is recognised for the D.C.H.

Applications, with copies of 2 testimonials, to the Secretary.

WINCHESTER. ROYAL HAMPSHIRE COUNTY HOS-PITAL. (311 Beds.) SENIOR HOUSE OFFICER (orthopædics) required immediately. Appointment for 6 months in the first instance.

Applications, with copies of 2 testimonials, to the Secretary.

WINCHESTER. ROYAL HAMPSHIRE COUNTY HOS-PITAL. (311 Beds.) HOUSE OFFICER (gynæcology) required, vacant mid-September. The hospital is recognised by the Royal College.

Applications, with copies of 2 testimonials, to the Secretary.

WINDSOR. KING EDWARD VII HOSPITAL. House SURGEON in general surgery required (Male or Female) for post vacant 14th August. Post recognised for F.R.C.S. Salary on national scale. Preference will be given to persons seeking a pre-registration House Officer post under the Medical Act, 1950.

Applications, with copies of recent testimonials, or names of 2 referees, stating age, qualifications with dates, and nationality, to be sent to the Hospital Secretary by 7th August.

WELSH REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of a REGISTRAR in General Surgery to serve the Cardiff Hospital Management Committee. The successful candidate will be based at Barry Accident Hospital, Barry, Glam. The post which will be subject to review at the end of the first year may be resident or non-resident. An unfurnished house can be made available for a married candidate.

Forms of application should be obtained from the Senior Administrative Medical Officer, Welsh Regional Hospital Board, Cathays Park, Cardiff, within 14 days of appearance of this advertisement.

WELSH REGIONAL HOSPITAL BOARD. North Wales CHILD GUIDANCE CLINICS. Applications are invited for the post of REGISTRAR for the above clinics which provide a comprehensive Child Guidance Service for the North Wales Area, under the direction of the full-time Consultant Child Psychiatrist. Clinics are held weekly at Bangor, Colwyn Bay, Rhyl and Wrexham. These are fully staffed. Experience of general practice or pædiatrics is desirable. Ability to speak Welsh would be an advantage. A close association exists between the clinics and the area Mental Hospital at Denbigh. There is ample opportunity for study and clinics and hospital are recognised for D.P.M. The post will be subject to review at the end of the first year.

Forms of application should be obtained from the Senior Administrative Medical Officer, Welsh Regional Hospital Board, Cathays Park, Cardiff, within 14 days of appearance of this advertisement.

WELSH REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of a REGISTRAR in Anæsthetics to serve the Glantawe Hospital Management Committee. The successful candidate will be based at Morriston Hospital, Morriston, near Swansea. The post may be either resident or non-resident and will be subject to review at the end of the first year.

Forms of application should be obtained from the Senior Administrative Medical Officer, Welsh Regional Hospital Board, Cathays Park, Cardiff, within 14 days of appearance of this advertisement.

WELSH REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of a REGISTRAR in General Medicine, including tuberculosis, at St. David's Hospital, Cardiff (656 Beds). The post is non-resident and will be subject to review at the end of the first year.

Forms of application should be obtained from the Senior Administrative Medical Officer, Welsh Regional Hospital Board, Cathays Park, Cardiff, within 14 days of appearance of this advertisement.

WESTON-SUPER-MARE GENERAL HOSPITAL. (110 Beds.) Applications are invited from registered medical practitioners for the resident appointment, vacant mid-August, of HOUSE SURGEON (first, second, or third post). The appointment will be for a period of 6 months in the first instance and may be renewed for a further 6 months.

Applications, stating age, qualifications and experience, together with names and addresses of 2 referees, should be addressed to the Secretary, Weston-super-Mare Hospital Management Committee.

WREXHAM. WAR MEMORIAL HOSPITAL. (170 Beds.) WREXHAM, POWYS AND MAWDDACH HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of HOUSE SURGEON at the above Hospital, to commence immediately. The appointment is recognised for the Diploma of F.R.C.S. (Eng. and Edin.), and is an approved pre-registration House Officer post. Salary will be at the rate of £350, £400 or £450 p.a. according to experience, less £100 p.a. for residential emoluments.

Applications, stating age, nationality, qualifications and experience, together with copies of 2 recent testimonials, should be addressed to—

WILLIAM JONES, Secretary, Wrexham,
Powys and Mawddach Hospital Management Committee.
Maelor General Hospital, Croesnewydd-road, Wrexham.

WREXHAM. WAR MEMORIAL HOSPITAL. (170 Beds.) Applications are invited for a PÆDIATRIC HOUSE OFFICER to commence duties immediately at the above Hospital. This Hospital has a Baby Unit of 15 Cots for acute cases and a busy Outpatients Department. Certain duties in the main general Pædiatric Unit of 50 Beds and Cots are also arranged by the Consultant Pædiatrician.

Applications, stating age, qualifications, and copies of 2 testimonials, should be sent to—

WILLIAM JONES, Secretary, Wrexham,
Powys and Mawddach Hospital Management Committee.
Maelor General Hospital, Wrexham.

WOKING AND CHERTSEY GROUP HOSPITAL MANAGEMENT COMMITTEE. ST. PETER'S HOSPITAL, CHERTSEY (430 Beds: late Botley Park War Hospital), and ROYAL SURREY COUNTY HOSPITAL, GUILDFORD (229 Beds). SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. The post of Full-time REGISTRAR to the E.N.T. Departments of the above hospitals will be vacant on 1st October, 1953.

Application forms can be obtained from, and should be returned by 22nd August to, the Group Secretary, Huntington, Guildford-road, Chertsey. The hospitals may be visited by arrangement (Tel. No's. : St. Peter's—Ottershaw 441 ; Royal Surrey County—Guildford 2323).

WORKINGTON INFIRMARY. (86 Beds plus Annexe 34 Beds.) WEST CUMBERLAND HOSPITAL MANAGEMENT COMMITTEE. HOUSE PHYSICIAN (pre-registration post) required. Post graded Senior House Officer or House Officer, under national scales, in accordance with experience of applicants.

Applications, stating qualifications with dates, and experience, and accompanied by copies of 2 testimonials, to be sent to the Secretary, Workington Infirmary, Workington, Cumberland.

WORCESTER (near). POWICK MENTAL HOSPITAL. Locum JUNIOR HOSPITAL MEDICAL OFFICER required.

Applications, with copies of testimonials, should be sent to the Medical Superintendent.

WORCESTER. RONKSWOOD HOSPITAL. Applications are invited for the appointment of Pre-registration HOUSE SURGEON (general surgery). The post will be tenable for 6 months and salary and conditions will be in accordance with the terms for hospital medical staff.

Applications, with copies of testimonials, should be sent to the Hospital Secretary.

WORCESTER. RONKSWOOD HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER in Surgery which is now vacant. The appointment is tenable for 1 year and is subject to the terms and conditions of service for hospital medical staff.

Applications, with copies of 3 testimonials, should be sent to the Hospital Secretary.

WORCESTER. RONKSWOOD HOSPITAL. Applications are invited for the post of RESIDENT ANÆSTHETIST which is now vacant. The post is of Senior House Officer status. The holder may expect a reasonable proportion of emergency work. Conditions in accordance with terms and conditions of service for hospital medical staff.

Applications, with copies of testimonials, should be sent to the Hospital Secretary.

WORCESTER ROYAL INFIRMARY. House Physician required as from 15th September for duties in acute general medical ward (including cardiology) and also in modern pædiatric ward. The appointment is tenable for 6 months and is subject to the terms and conditions of service for hospital medical staff.

Applications, with copies of testimonials, should be sent to the Secretary.

WORCESTER ROYAL INFIRMARY. Applications are invited for the post of HOUSE SURGEON (general surgery/orthopædics) which becomes vacant beginning September. The appointment is tenable for 6 months and is subject to the terms and conditions of service for hospital medical staff.

Applications, with copies of testimonials, should be sent to the Secretary.

WOLVERHAMPTON HOSPITAL MANAGEMENT COMMITTEE GROUP NO. 16 BIRMINGHAM REGION.

The Royal Hospital, Wolverhampton (an Associated Hospital of the University of Birmingham Medical School)
SENIOR HOUSE OFFICER or HOUSE OFFICER (Fracture and Orthopædic Department), vacant now.
HOUSE OFFICER (anæsthetics), vacant now. Appointment recognised for D.A.
HOUSE OFFICER (Casualty Department), vacant now.

Wolverhampton and Midland Counties Eye Infirmary
HOUSE OFFICER, vacant now. Appointment recognised for F.R.C.S. and D.O. examinations.

Applications, with copies of 3 recent testimonials, to be sent to W. COCKBURN, Group Secretary.
The Royal Hospital, Wolverhampton.

YORKSHIRE. EAST RIDING HOSPITAL MANAGEMENT COMMITTEE.

Westwood Hospital, Beverley, Yorks (218 Beds)
(*a*) ORTHOPÆDIC HOUSE SURGEON (Senior House Officer). Recognised for F.R.C.S. Vacant now.

East Riding General Hospital, Driffield, Yorks (249 Beds)
(*b*) HOUSE SURGEON (first, second, or third post), vacant now. Pre-registration post. Recognised for F.R.C.S. General surgical duties.

Salary for (*a*) is £670 p.a., less £140 for board and lodging ; and for (*b*) £350–£450 p.a., less £100 for board and lodging. Fully qualified practitioners may also apply for the pre-registration post.

Detailed applications to Secretary, Westwood Hospital, Beverley, Yorkshire.

CHANNEL ISLANDS, JERSEY. GENERAL HOSPITAL. Applications are invited for the post of RESIDENT SURGICAL OFFICER at the above Hospital. Previous experience is essential. The Hospital has 200 Beds and is recognised as a training Hospital for the F.R.C.S. Post is vacant on 1st October, 1953. The appointment is for 6 months in the first instance, but is renewable for a further 6 months. Salary £700 p.a., less £100 for residential emoluments.

Applications to be submitted not later than 22nd August, 1953, to the President, Public Health Committee, General Hospital, Jersey, C.I.

DOUGLAS. NOBLE'S ISLE OF MAN HOSPITAL. (160 Beds.) Applications are invited for the post of HOUSE PHYSICIAN at this busy Hospital. The post which is now vacant offers varied experience in pleasant surroundings. 4 residents on the staff. Salary £350, £400, or £450 a year, according to experience. A deduction of £100 a year made in respect of residential emoluments. The appointment is for 6 months in first instance.

Applications, stating full details, with copies of 2 recent testimonials, to the Secretary, Noble's Hospital, Douglas, Isle of Man.

DOUGLAS. NOBLE'S ISLE OF MAN HOSPITAL. (160 Beds.) Applications are invited for the post of HOUSE SURGEON at this busy general hospital. The post becomes vacant at the end of August, 1953, and offers wide experience in congenial surroundings. Salary at the rate of £350, £400, or £450 a year according to experience, subject to a deduction of £100 a year in respect of residential emoluments. 4 residents on the staff. The appointment is tenable for 6 months in the first instance.

Applications, giving full particulars, with copies of 2 recent testimonials, to the Secretary, Noble's Hospital, Douglas, Isle of Man.

DOUGLAS. NOBLE'S ISLE OF MAN HOSPITAL. (160 Beds.) Applications are invited for the post of RESIDENT ANÆSTHETIST at this busy Hospital. The post, which becomes vacant at the end of August, 1953, offers varied experience in pleasant surroundings. 4 residents on the staff. Salary at the rate of £350, £400, or £450 a year according to experience. A deduction of £100 a year made in respect of residential emoluments. Duties may include acting in the medical wards or casualty. The appointment is tenable for 6 months in the first instance.

Applications, giving full particulars, with copies of 2 recent testimonials, to the Secretary, Noble's Hospital, Douglas, Isle of Man.

NORTHERN IRELAND FEVER HOSPITAL MANAGEMENT COMMITTEE. RESIDENT HOUSE PHYSICIANS (2) required immediately.

Applications to the Secretary, Northern Ireland Fever Hospital Management Committee, Purdysburn, Belfast.

BRITISH WEST INDIES. UNIVERSITY COLLEGE HOSPITAL OF THE WEST INDIES. Applications are invited from suitably qualified medical practitioners for the posts of RESIDENT CASUALTY PHYSICIAN and RESIDENT CASUALTY SURGEON at the above-named Hospital. This is a general teaching hospital of 300 Beds approved by the London University for its degrees. The appointments are for 1 year as from 1st November, 1953. Salary £670 p.a., less £100 for board, residence, &c. Single accommodation only is provided. Return first-class passages by sea will be paid.

Applications, stating nationality, age, qualifications with dates, and details of previous appointments, together with the names and addresses of 3 referees, or 3 testimonials in lieu thereof, should be sent to the Hospital Manager and Secretary, University College Hospital, Mona P.O., Jamaica, B.W.I., before 29th August, 1953.

NEW ZEALAND. THE OTAGO HOSPITAL BOARD. SENIOR ANÆSTHETIC REGISTRAR, Dunedin Hospital, New Zealand, ASSISTANT LECTURER in Anæsthetics, University of Otago. Applications are invited for the above position, from those who hold a degree in Medicine of an approved University. The appointment is a full-time one commencing on 1st January, 1954. Salary scale in accordance with the Hospital Employment (Medical Officers') Regulations, 1952, viz. : £863 15s.–£978 15s. p.a., plus £179 8s. p.a. living-out allowance. Further information relating to this appointment may be obtained from the Office of the High Commissioner for New Zealand, 415, The Strand, London, W.C.2, or from THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Applications, stating age, qualifications, and postgraduate experience, together with testimonials, health and radiological certificates, should be in the hands of the Secretary of the Board not later than 10 A.M. on Monday, 24th August, 1953.

W. A. WILLIAMSON, Secretary.

P.O. Box 946, Dunedin, New Zealand.

CANADA. WOMEN'S COLLEGE HOSPITAL, Toronto, CANADA. Applications from Women are invited for the REGISTRARSHIP at the Women's College Hospital, Toronto, Ontario, Canada. This is a 150-Bed hospital which is in the process of expansion, staffed entirely by women. Work consists of supervision of Junior House Doctors, experience in surgery and medicine and also some obstetrics. Salary of $100 per month paid. Tourist passage would be paid one way for chosen applicant.

Address application to Miss DOROTHY MACHAM, Superintendent.

Women's College Hospital.

NEW YORK. NEW ROCHELLE HOSPITAL, New ROCHELLE, NEW YORK, U.S.A. (360-Bed general community hospital.) Approved by American College of Surgeons; American Medical Association for Interneship and Residency Training. Only graduates from approved university schools accepted. INTERNES—$100 per month, plus full maintenance.

Apply Superintendent.

Public Appointments

HER MAJESTY'S COLONIAL SERVICE, Trinidad. MEDICAL OFFICERS OF HEALTH required. Duties include matters relating to sanitation, public-health education, venereal diseases, tuberculosis, maternity and child welfare, school medical work, housing and town planning. Appointments can be made on a permanent basis with pension (non-contributory) at the age of 55, or on short-term agreement. A candidate in the National Health Service may resign from the National Health Service but retain his superannuation rights during his time in Trinidad (up to 6 years) and receive a resettlement grant of 20% of the aggregate of his Trinidad salary on leaving Trinidad at the end of his engagement. Salary scale ranges from B.W.I.$5280 to B.W.I.$5760 (£1100–£1200) p.a. A temporary variable cost-of-living allowance is at present payable at the rate of $108 p.a. (1 B.W.I.$ equals 4s. 2d.). Starting salary is determined in accordance with the candidate's age, qualifications and experience. Pension is earned at the rate of 1/600th of the final pensionable emoluments for each completed month of service. Provision of quarters not guaranteed, but if government quarters are provided a small rental is charged. Where government quarters are not provided an allowance in lieu is payable. Free passages on first appointment are provided for Officer and family not exceeding 5 persons in all, also free passages on leave subject to a maximum of 3 adult fares. Income-tax at local rates. Local leave is permissible and generous home leave is granted after each tour. Tour of service is 3½ years. Educational facilities are available. Candidates must possess qualification registrable in the United Kingdom and must also hold the Diploma in Public Health.

Application forms can be obtained from the Director of Recruitment (Colonial Service), Colonial Office, Sanctuary Buildings, Great Smith-street, London, S.W.1 (quoting reference No. CDE.117/38/04).

HER MAJESTY'S COLONIAL SERVICE. Hong-Kong. SPECIALIST (Anæsthetist) required in the Medical Department of Hong-Kong for general anæsthetic duties and training of local Anæsthetists. Appointment will be on 2 years probation for permanent and pensionable employment. Salary including pensionable expatriation pay is $2663.33 per mensem (£1997 10s. p.a.—1 Hong-Kong dollar equals 1s. 3d.). A temporary, non-pensionable, cost-of-living allowance of from $228 to $570 per mensem according to family circumstances is also paid. Free passages in both directions are provided for Officer, wife, and up to 3 children under the age of 18 years. Quarters if available, are provided at reasonable rental. Income-tax at local rates. Local leave is permissible and generous home leave is granted after each tour of 4 years duration. Normal retiring age is 55 and pension is earned at the rate of 1/600th of the final pensionable emoluments for each completed month of service. Climate is favourable for Europeans. Educational facilities are available. Candidates must possess medical qualifications registrable in the United Kingdom and a Diploma in Anæsthetics. They must also have been qualified for 7 years, of which 5 years must have been spent working in anæsthetics.

Application forms can be obtained from the Director of Recruitment (Colonial Service), Colonial Office, Sanctuary Buildings, Great Smith-street, London, S.W.1 (quoting reference No. CDE.117/51/09).

HER MAJESTY'S COLONIAL SERVICE. Fiji. RADIOLOGIST is required to take charge of X-ray Department of the Colonial War Memorial Hospital in Suva, to undertake occasional X-ray duties at the Tamavua Tuberculosis Hospital and to advise in the operation and maintenance of other X-ray units in Fiji. Other duties will include training of locally recruited personnel as Assistant Radiographers and assisting with teaching and lectures at the Central Medical School. Appointment on permanent basis with pension (non-contributory) at the age of 55. Salary scale ranges from £F1550 p.a. to £F1650 p.a. (£F111 equals £100 sterling). Starting-point in the salary scale is determined according to qualifications and experience. A temporary cost-of-living allowance at 10% of salary, subject to a maximum of £F130 p.a., is also payable. Pension is earned at the rate of 1/600th of the final pensionable emoluments for each completed month of service. Quarters, if available, are provided at low rental. Free passages, on appointment, are provided for Officer and family up to the cost of 4 adult fares, and, on leave, up to the cost of 3 adult fares. Income-rax at local rates. Generous home leave is granted after each tour of from 2 to 3 years. Candidates must possess medical qualification registrable in the United Kingdom and the D.M.R.E. or D.M.R.D.

Application forms may be obtained from the Director of Recruitment (Colonial Service), Colonial Office, Sanctuary Buildings, Great Smith-street, London, S.W.1 (quoting reference No. CDE.117/162/02).

HER MAJESTY'S COLONIAL SERVICE. Nigeria. Applications are invited from Doctors with medical qualifications registrable in the United Kingdom and with at least 1 years experience after qualification for the following posts in the Medical Department of the Government of Nigeria :—

(*a*) MEDICAL OFFICERS, for general duties in preventive and curative medicine which may include purely rural health work, involving much travelling.

(*b*) MEDICAL OFFICERS OF HEALTH. Duties as under (*a*). In addition the selected officers would undertake the control of sanitary matters, and may be required to perform the duties of Port Health Officer at a sea or air port. Candidates should possess a Diploma in Public Health. A Diploma in Tropical Hygiene, though not essential, is desirable.

Appointments may be made as follows :—

(*a*) on 3 years probation for permanent and pensionable employment in the Colonial Medical Service, with retiring age of between 45 and 55. Pensions are at the rate of 1/600th of final pensionable emoluments for each completed month of reckonable service ;

(*b*) from the National Health Service. Candidates may resign from the National Health Service but retain their superannuation rights during their time in Nigeria (up to 6 years) and receive a resettlement grant of 20% of the aggregate of their Colonial salary on leaving Nigeria at the end of their engagement ; or

(*c*) on short-term contract (2–4 tours of 18 months duration) with inclusive salary of from £1087 p.a. rising to £2000 p.a. ; on completion of contract a gratuity is paid at the rate of £37 10s. for each completed period of 3 months service (including leave).

Officers appointed under (*a*) or (*c*) are required to contribute to a Widows' and Orphans' Pension Scheme. Salaries, including pensionable expatriation pay for Officers appointed under (*a*) or (*b*) range from £950 to £1850 p.a. Starting salary in all cases depends on experience and war service. Quarters are provided at low rents. Free passages in both directions are provided for Officer and his wife. Payment of the cost actually incurred on 1 outward and 1 homeward passage for each of 2 children under age of 18, subject to maximum of £75 in respect of the return journey for each child, is also granted. Income-tax at local rates. Local leave is permissible and generous home leave is granted after each tour of 18 months duration.

Application forms can be obtained from the Director of Recruitment (Colonial Service), Colonial Office, Sanctuary Buildings, Great Smith-street, London, S.W.1 (quoting reference No. CDE./117/14/01).

LANCASHIRE COUNTY COUNCIL. Registered medical practitioners required for appointment of ASSISTANT DIVISIONAL MEDICAL OFFICERS in areas adjacent to Blackburn, Bury, Fleetwood, Ormskirk/Southport. Possession of D.P.H. desirable. Salary £950–£50–£1300 p.a. Travelling and subsistence allowances where applicable. Posts superannuable and subject to medical examination.

Application form and further particulars obtainable from County Medical Officer, East Cliff County Offices, Preston.

BOLTON. COUNTY BOROUGH OF BOLTON. Appointment of ASSISTANT MEDICAL OFFICER OF HEALTH AND ASSISTANT SCHOOL MEDICAL OFFICER. Applications are invited for the above appointment from suitably qualified registered medical practitioners (Male or Female). The duties will be mainly in connection with the Maternity and Child Welfare Service and School Health Service, but the person appointed will be expected to carry out such other duties as may from time to time be allotted by the Medical Officer of Health. The possession of a D.P.H., D.C.H., or D.Obst.R.C.O.G. is desirable but not essential. The salary scale for the post is £950–£50–£1300. In fixing the commencing salary consideration will be given to previous experience and to the possession of higher qualifications. The appointment will be superannuable, and the successful candidate will be required to pass a medical examination. The appointment will be terminable by 3 months notice on either side. There are no forms of application, but further particulars may be obtained from the Medical Officer of Health, Civic Centre, Bolton.

Applications, giving full particulars of age, qualifications and experience, and the names and addresses of 3 persons to whom reference may be made, should be forwarded to the undersigned not later than 6th August, 1953.

Town Hall, Bolton. PHILIP S. RENNISON, Town Clerk.

BIRMINGHAM. CITY OF BIRMINGHAM. Public HEALTH DEPARTMENT. Applications invited for appointment of Whole-time DENTAL OFFICER (Male or Female). Duties will be concerned with dental inspection and treatment of expectant and nursing mothers, and young children up to age of 5 years. Salary £800–£50–£1250 p.a. with placement on the scale according to experience. Pension scheme (including Widows and Orphans); medical examination. The Officer appointed will be required to devote his/her whole time to official duties and the appointment will be subject to 1 months notice on either side.

Applications, stating qualifications and experience, with names of 3 referees, to be sent to Medical Officer of Health Council House, Birmingham, 3, not later than 17th August, 1953.

BIRMINGHAM. CITY OF BIRMINGHAM. Public HEALTH DEPARTMENT. Applications invited from registered medical practitioners for post of ASSISTANT ADMINISTRATIVE MEDICAL OFFICER OF HEALTH (Male or Female). Candidates should hold the Diploma of Public Health. The successful candidate will have an opportunity to gain experience in all branches of the Public Health Service, including maternity and child welfare. The salary scale, as at present laid down —i.e., £1050 rising by £50 annually to £1250 p.a.—is receiving consideration in the light of the recent award to Assistant Medical Officers. Commencing salary within the agreed scale will depend upon the Medical Officer's experience. The appointment will become vacant towards the end of September. Pension scheme; medical examination. The Officer appointed will be required to devote his/her whole time to official duties and the appointment will be subject to 1 months notice on either side.

Form obtainable from Medical Officer of Health, Council House, Birmingham, 3. Applications, stating qualifications and experience, with names of 3 referees, to be sent to Medical Officer of Health, Council House, Birmingham, 3, not later than 17th August, 1953.

FACTORY DOCTORS. Factories Acts, 1937 and 1948. The following appointment as Appointed Factory Doctor is vacant. Apply to Chief Inspector of Factories, 8, St. James's-square, London, S.W.1.

District	*County*	*Latest date for receipt of applications*
CHULMLEIGH ..	DEVON ..	15TH AUGUST, 1953

TREASURY MEDICAL SERVICE. Applications are invited from medical practitioners, practising in the districts detailed below, for appointment in a part-time and mainly advisory capacity as LOCAL TREASURY MEDICAL OFFICER for each of the places or groups of places shown. The town shown in parentheses after the place-names indicates the Head Post Office Area in which the place, or group of places, is situated. Successful applicants will be required to examine and report on the condition of certain Government Officers, teachers, candidates for appointment, &c., who may be referred to them from time to time; and to attend when summoned to an emergency case of accident or sudden illness occurring in a Government office in the neighbourhood. Fees for this work, and mileage allowance where necessary, will be paid on a scale agreed with the British Medical Association.

Intending applicants should write, within 14 days, to Treasury Medical Adviser, Treasury Chambers, Whitehall, S.W.1, for a form on which application may be made. Applicants should be not more than 60 years of age.

The places for which applications are invited are as follows :—

ENGLAND AND WALES

Evercreech (Shepton Mallet).
West Wimbledon (London), S.W.20.
Plympton (Plymouth).
Lakenheath (Thetford).
Oakengates and Shifnal (Wellington Salop).
Wisbech (Wisbech).

SCOTLAND

Drumbeg, Elphin, Kylesku and Lochinver (Lairg).

General Practice

For an Executive Council post (England and Wales) apply on form E.C.16A obtainable from the council. Mark envelope "Vacancy."

DEVORAN, CORNWALL. Applications invited for a resignation VACANCY (rural) to take effect on 30th September next. No living-accommodation but surgery may be available. List at present approximately 1250, practically all dispensing. Applications on Form E.C.16A to reach the undersigned on or before 15th August, 1953.

F. A. PENROSE, Clerk, Cornwall Executive Council.
Benson House, Moresk-road, Truro, Cornwall.

Hospital Services : Non-Medical Appointments

WOLVERHAMPTON HOSPITAL MANAGEMENT COMMITTEE GROUP NO. 16 BIRMINGHAM REGION. THE ROYAL HOSPITAL, WOLVERHAMPTON (an Associated Hospital of the University of Birmingham Medical School). PATHOLOGICAL LABORATORIES. BIOCHEMIST required to take charge of Department. Terms of employment and salary in accordance with Whitley scale.

Applications, with full details of qualifications and experience, to the Secretary.

Appointments : Too Late for Classification

REGIONAL NEUROSURGICAL CENTRE. (50 Beds.) BROOK GENERAL HOSPITAL, Shooters Hill-road, S.E.18. SENIOR HOUSE OFFICER (neurosurgery), vacant 16th September. The post, which is recognised for F.R.C.S., also provides excellent opportunity for training in neurology. Salary £670 p.a., less £150 p.a. for residence.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

ST. NICHOLAS HOSPITAL, Plumstead, S.E.18. House SURGEON (gynæcology and obstetrics), vacant now. Application is being made for recognition for M.R.C.O.G.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

ST. NICHOLAS HOSPITAL, Tewson-road, Plumstead, S.E.18. SENIOR HOUSE OFFICER (anæsthetics), vacant October. 6 months appointment and may then be renewed. Recognised for D.A. Salary £670 p.a., less £150 p.a. for residence.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

NORTH SHIELDS. TYNEMOUTH VICTORIA JUBILEE INFIRMARY, Hawkey's-lane, NORTH SHIELDS, NORTHUMBERLAND. (109 Beds.) HOUSE SURGEON (pre-registration), appointment available now. Salary and conditions in accordance with national terms.

Applications to House Governor.

Miscellaneous

To non-professional posts the Notification of Vacancies Order 1952 applies

Ciba Laboratories Ltd., Horsham, require the whole-time services of a well-qualified Doctor, preferably under 35, whose primary duty will be to act as liaison between the company (which in the U.K. represents Ciba as a world concern) and centres of research in organising clinical trials throughout the U.K. of products of Ciba research. He will not himself do research but should have the closest contact with those who do. He will otherwise advise and help in medical matters. Starting salary according to age and qualifications but not less than £1200 plus free flat. Excellent Pension Fund.—Send age, full particulars of career, reason for application and other relevant details to the Managing Director.

AMENDED ADVERTISEMENT

Gold Coast. Port of Tema. During the construction of this port the Consulting Engineers require a British medical officer with experience in tropical diseases, preferably associated with labour forces. Contract 12–15 months, renewable after 2 months leave; project 4 years. Salary £2000–£2500 p.a., according to qualifications, with free furnished quarters, transport and passage, including wife, and children below 14 years. Duties include planning and organisation of medical facilities as well as clinical and administrative work of hospital to be built.—Applications (closing date 29th August, 1953), quoting 3 names for reference purposes, to: Address, No. 834, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Radiotherapist. There is a vacancy for an Assistant, with a view to a partnership, in South Africa. The salary during the period of assistantship, and the terms of the partnership, will depend on experience and qualifications. The commencing salary offered is £2500–£3500, depending on qualifications. Applicants should have the necessary qualifications for the Register of Specialists in South Africa. Full personal and professional details are requested. The Advertiser will be available for interviews in London, from the middle of August to the middle of September.—Address, No. 824, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

B.W.I.—Excellent opening in major B.W.I. Island for experienced General Practitioner. Ample scope for specialties, appointments, and hospital facilities. Premises, equipment, drugs, and furniture for sale. Introduction given. Principal taking up full-time appointment.—Write, Box N.466, c/o STREETS, 110, Old Broad-street, E.C.2.

Young Lady (23), Social Science and Secretarial qualifications, seeks post with G.P.s as Secretary.—Address, No. 843, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Consulting-rooms, full and part time, and Houses in the medical area.—ELGOOD & Co., 1, Bentinck-street, W.1 (WELbeck 8974).

For Sale. Cambridge Standard Electro-cardiograph. A.c. model, complete with all accessories. New in 1947. Cost £266.—Offers to: Address, No. 844, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

"Pregnancy Diagnosis by the Xenopus Method." 24-hour service.—Send specimen of urine and £1 1s. fee to: WELBECK BIOLOGICAL LABORATORIES, 26, Park-crescent, Portland-place, W.1 (Telephone: MUSeum 5386–7).

Applicants for posts requiring testimonials copied or duplicated should communicate with MANTON SECRETARIAL SERVICE, LTD., 98, Victoria-street, S.W.1 (Phone: VICtoria 0141), who are specialists in this kind of work.

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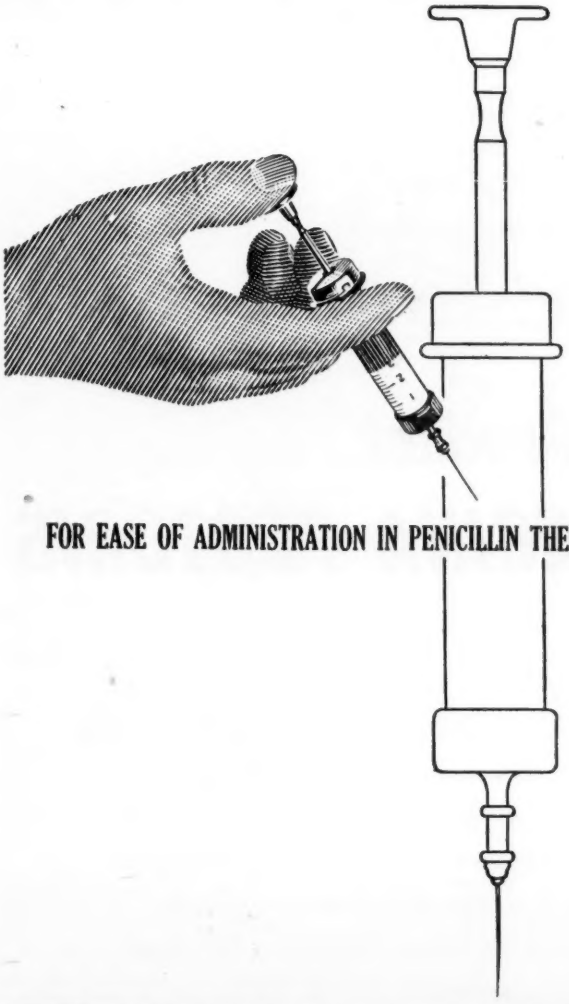

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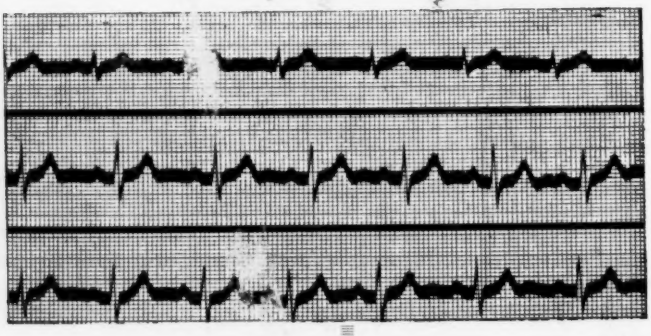

A New Bayer Product

FOR THE TREATMENT OF ANGINA PECTORIS

In angina pectoris, 'Mycardol'* reduces the severity of the attacks and may help to diminish their frequency while, at the same time, improving exercise tolerance. Especially valuable in reducing the need for repeated doses of trinitrin, and of extremely low toxicity, this long acting nitrite provides a new and important adjuvant in the routine management of angina pectoris.

* Pentaerythritol tetranitrate.

Mycardol

Trade Mark

Packings: tablets of 30 mg., (scored to give 15 mg. per half tablet), in bottles of 100 and 1,000 tablets. The basic N.H.S. price of one week's treatment is 1/6d.

Literature will gladly be sent upon request.

Manufactured in England by

BAYER PRODUCTS LIMITED

Africa House, Kingsway, London, W.C.2

Associated export company: WINTHROP PRODUCTS LIMITED, London